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A NOTE ON THE VERMIFORM APPENDIX

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The appendix is a vestigial organ serving no useful purpose' (Ackermann[1] 1914). This statement appears in many textbooks and, moreover, is held to be true by many teachers of medicine. As early as 1903, Metchnikoff in his famous book 'The Nature of Man' wrote, 'It is no longer rash to say that not only the rudimentary appendix and caecum, but the whole of the large bowel are superfluous and that their removal would be attended with happy results'. As recently as 1953 Patten[2] stated that the appendix was a phylogenetically decadent structure. The purpose of this article is to re-examine some of the facts and renew interest in a maligned but persistent phylogenetic organ.

Embryology

Primary differentiation of the appendix from the caecum occurs at the 7th-8th week of embryonal life, when growth in the most dependent part of the caecum tends to lag, that part actually decreasing in size. In the 6th-month foetus the future appendix is a third of the diameter of the large bowel. At birth, the differentiation of caecum and appendix becomes more striking as the longitudinal muscle bands separate and the circular muscles of the colon expand to form the colonic haustra. After birth the caecum tends to expand not only because of its inherent growth, but also because as the individual assumes an upright posture gravity tends to hold the pre-faecal contents in the caecum. At maturity the ratio of diameter of appendix to that of caecum is reduced to about 1:8.

A description of a 'transient appendix' by Kelly and Hurden[3] (1905) is rarely featured in embryological studies. They studied the developing caeco-appendix in over 50 young human embryos and found 'a remarkable growth from the tip of the caecum, which simulates in its position and form the true appendix'. This grows during the 6th week and atrophies afterwards toward the end of the 7th week or so. Here then is a definite embryological origin for the development of a supernumerary appendix.

Comparative Anatomy and Evolution of the Appendix

Berry[4] (1900) in his classical paper showed that the vermiform appendix of man is a specialized part of the alimentary canal. He found in his study of many vertebrate types that the amount of lymphoid tissue in the caecum is largely in excess of that contained in other parts of the large intestine. In fact the tendency for lymphoid tissue to be specially collected together into a differential part of the alimentary canal becomes more marked in certain groups of the vertebrate series. In the pigeon, goose and fowl, the lymphoid tissue occupies the whole length of the caecal wall. In the mouse and rat there is an attempt at constriction in the caecum, and the lymphoid tissue is confined to the apical part. In the rabbit this constriction has become much more clearly defined, there being both a caecum and an appendage, the latter containing large quantities of lymphoid tissue, whilst the caecum has but little.

In the primates[5] an appendix is found in both major subdivisions. In the *Strepsirhini* the caecum is large and ends in a process simulating a vermiform appendix, both macroscopically and histologically, although it is not always sharply demarcated from the rest of the organ. In the *Haplorhini* the caecum is short, and only in *Hominidae* (modern and extinct man), *Pongidae* (gorilla, chimpanzee) and *Hylobatidae* (gibbon) is the apex specially modified to form a vermiform appendix. Nevertheless, in all the other subgroups there is specialized development of lymphoid nodules in the apical region of the caecum.

From the above data two facts are clear:

1. Although an appendix is found in almost all the primates, it appears in its highest form of development in those that have assumed the upright posture, culminating in man.

2. We know from their fossil remains that the great anthropoids are of extreme geological antiquity; was the appendix injurious or vestigial in them, there has been ample evolutionary time to accomplish its suppression. Keith[6] (1912) supported this contention. He stated: 'So like are the caecum and appendix of the gorilla and chimpanzee to the same structures in man, that I know of no character by which an expert could tell them apart. In the anthropoid as in man the caecum and appendix undergo the same peculiar changes in passing from infancy to adult age.'

Johnston[7] (1920) maintained that the human caecum was in a state of retrogression. Nevertheless, he admitted the appearance of the vermiform appendix as a structure mainly lymphoid in nature and specially developed. Romer[8] (1955) also denies that the appendix is vestigial in nature. In short, all evidence suggests that, contrary to its being a vestigial

organ, the appendix is in fact a specialized part of the human bowel.

The chief stumbling block to the acceptance of this theory has been the failure to ascribe any definite function to the appendix.

Physiology

However, Wangensteen et al.[9] (1937) have shown that the appendix secretes 1-2 c.c. of fluid daily, this being a secretion and not a filtrate, since it can be collected from an unobstructed appendix. Mucus, calcium, phosphates, and digestive enzymes are present in the secretion. Not much is known about its movements. Peristalsis due to stimulation *in situ* has been observed by some. If an exteriorized appendix is stimulated it shows slow contractions lasting several minutes; the longitudinal muscle contracts first to cause shortening, then circular muscle contracts, reducing the size of the lumen.

These experiments serve to indicate that the appendix is an active, functioning organ, structurally and physiologically equivalent to the adjacent intestine, and hardly a 'vestige' in the true sense.

Discussion

From a consideration of all the evidence it can be reasonably assumed that the vermiform appendix of man is neither vestigial nor in a state of retrogression, but that it is in fact a specialized lymphoid structure with all the functions of lymphoid tissue elsewhere in the body. It appears to be a sentinel gland situated at the commencement of the large bowel. At the ileocaecal junction the alimentary tract changes from a relatively sterile structure to one laden with bacteria. The appendix may well be a barrier against the retrograde invasion of the small bowel by such colonic bacteria.

Young[10] (1957) considered that the appendix in mammals is concerned with the neutralization of bacterial toxins. Furthermore he states that 'in man and other mammals with a reduced caecum, the appendix perhaps retains some anti-bacterial functions, though it can be removed without any evident ill-effects'.

SUMMARY

1. Comparative anatomical studies indicate that the appendix is a specialized organ.

2. Notes on the embryology and physiology of the appendix are included

I am indebted to Dr. R. Singer, of the Department of Anatomy, University of Cape Town, for his helpful criticism and assistance.

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EDITORIAL

TROUBLE AFTER CHOLECYSTECTOMY

Cholecystitis, with or without gall-stones, is a very common condition in South Africa, and cholecystectomy, by the same token, is undertaken frequently in all parts of the country. The occurrence of symptoms after this operation which, by reason of the patient's bulk and the anatomical arrangements at the common bile-duct, is often one of no small severity, is always a great disappointment and a source of frustration and anxiety to the patient and of irritation to the surgeon.

In an article considering the symptoms after cholecystectomy, Burnett and Shields have analysed 200 cases.[1] Of these, 141 patients have been traced, of whom 134 (95%) had had very severe pain before operation, from either biliary colic or acute cholecystitis. The authors assure us that the viscus was never removed unless stones were present or the wall of the gall-bladder was obviously diseased; with this admirable policy of restraint—one well worthy of imitation—no reasonable surgeon can find fault. Twenty patients had significant symptoms after the operation, of whom 18 had the cause finally traced to an extrabiliary lesion; in only 2 cases could the symptoms be attributed to the operation—in both they were due to adhesions which resulted in kinking of the common bile-duct. Stenosis of the sphincter of Oddi was found twice, pancreatitis once and recurrent stones in the duct once. Thes figures should be encouraging to surgeons.

The authors conclude that most of the symptoms that occur after cholecystectomy carried out for stones or for definite disease of the gall-bladder wall are not due to biliary dyskinesia and that the use of the term post-cholecystectomy syndrome is no longer justified.

As long ago as 1925 Judd[2] commented on the not infrequently poor results that are obtained after cholecystectomy where stones are not present. This can be confirmed by the experience of most practising surgeons, who are well aware of the disappointments that follow over-enthusiastic removal of an organ containing no stones through whose thin wall the clear bile appears blue-green.

We may safely say that today the main difficulty where the disease is restricted to the gall-bladder is entirely anatomical and the risk of injury to the common bile-duct the main hazard. Glenn,[3] however, in a careful analysis of mishaps during cholecystectomy, has pointed out that not a single case of injury to the common bile-duct was encountered when the removal of the viscus was begun at the fundus and carried on towards the duct; and this information deserves to be widely disseminated. Inexperienced operators or those who may be called on to perform cholecystectomy where conditions are not ideal should know and be comforted by this simple piece of technical information. The consequences of injury to the common bile-duct are so depressing that there can be little justification for performing a type of operation in which the risk of its gravest complication can be avoided by a relatively simple alteration in technique. It is all very well for the expert to delight his colleagues in exhibitions of operative dexterity, but for the majority 'simple surgery for simple surgeons' should surely be the goal at which to aim.

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VAN DIE REDAKSIE

AFRIKAANS AS MEDIESE VAKTAAL

Onder die opskrif *Afrikaans in Ons Blad* het dr. C. L. Leipoldt,[1] destyds redakteur van die S.A. Tydskrif vir Geneeskunde, reeds in 1944 daarop gewys dat dit noodsaaklik geword het om eenstemmigheid te bereik ten opsigte van Afrikaanse mediese vakterme. Wat tot hierdie skrywe van dr. Leipoldt aanleiding gegee het, was, onder andere, die skerp kritiek wat gevolg het op die verskyning van die Voorlopige Geneeskundige Woordelys.

Die toestand van sake waarna dr. Leipoldt verwys het, bly vandag nog min of meer onveranderd; ook het die situasie na aanleiding waarvan hy geskryf het, homself onlangs weer herhaal. In 1944 het die woordelys waarna ons hierbo verwys het, verskyn, en skerp kritiek het daarop gevolg. In 1953 het die lys van *Afrikaanse Ontleedkundige Terme* verskyn op gesag van die Direkteur van die Vaktaalburo van die S.A. Akademie vir Wetenskap en Kuns, en weer was daar skerp kritiek daarop.[2] En, gedurende die afgelope aantal jare, het die mediese skool van die Universiteit van Stellenbosch op die toneel gekom met skryf- en spelgebruike van mediese vakterme wat skynbaar afwyk van sommige van die gebruike wat op hierdie gebied geld aan die mediese skool van Pretoria.

Ons sou die hele saak kon opsom deur te sê dat terwyl Afrikaans as algemene kultuurtaal sodanig geryp het dat dit op letterkundige gebied bydraes kon maak wat met trots vergelyk kan word met die beste in die wêreld, sekere gebiede van die vakterminologie—veral wat betref mediese vakterme—nog 'n ope gebied bly.

Wat die gebruik van Afrikaans as mediese vaktaal betref, het ons op die oomblik 'n paar enigsins uiteenlopende gebruiksrigtings. In die eerste plaas is daar die rigting (veral wat die basiese ontleedkundige terme betref) wat vertaling (verdietsing, en meer spesifiek, verafrikaansing) van terme voorstaan. Aan die anderkant is daar die rigting wat meer doelbewus ingestel is op 'n poging om sover moontlik aansluiting te vind by die gebruike van die *Internasionale*

terminologie. En in die derde plek is daar 'n soort tussenrigting wat die basiese internasionale vorm nie vertaal nie, maar verafrikaans. Op grond van hierdie drie skryfgebruike sou dieselfde orgaan om die beurt byvoorbeeld as baarmoedernek, cervix en serviks geskryf kon word.

Nou hoef die toestand soos hierbo geskets, niemand te verontrus of te ontmoedig nie. Dit weerspieël noodsaaklike en onvermydelike aspekte van die organiese groei van 'n jong en lewenskragtige taal. Maar, ons het nou tog 'n stadium bereik waar versigtige en verstandige leiding, op die basis van gedurige onderlinge bespreking en onderhandeling, baie nodig geword het.

Vir ons wil dit dus voorkom of die volgende stap behoort te wees om 'n raadplegende liggaam in die lewe te roep—nie noodwendig met die doel om onmiddellike eenstemmigheid te probeer verkry nie—want dit sou skaars moontlik wees, maar met die doel om langs die weë van gedurige raadpleging en onderhandeling stap vir stap bereikte ooreenkomste te finaliseer en te boekstaaf.

So 'n raadplegende kommissie sou byvoorbeeld kon bestaan uit mediese verteenwoordigers van die twee Afrikaanse mediese skole; 'n paar suiwer taalkundiges, insluitende verteenwoordigers van die S.A. Akademie vir Wetenskap en Kuns, en van die personeel van die Afrikaanse woordeboek; 'n paar ander raadgewers wie se liefde vir die saak, en kwalifikasies, hulle geskik maak om as raadgewers in hierdie verband op te tree, en 'n verteenwoordiger van die redaksionele personeel van die S.A. Tydskrif vir Geneeskunde. So 'n kommissie sou wel kon, maar hoef nie noodwendig, as geheel op gereelde tye te vergader nie. Maar dit sou kon dien as 'n belangrike raadgewende liggaam wat die organiese groei van Afrikaans as mediese vaktaal oor die loop van die volgende aantal jare in gesonde kanale sou kon stuur.

Ons wil almal wat in hierdie saak belangstel, uitnooi om daaroor te skryf en om wenke en raadgewing te stuur. Die doel wat ons voor oë moet hou, is die geleidelike skepping en standaardisering van Afrikaans as mediese vaktaal sodat die mediese studente wat deur die medium van Afrikaans opgelei word, niks verloor nie, en sodat die mediese vakterminologie nog 'n faset kan word van die algemene kultuurbydrae van die Afrikaanse taal.

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HAEMODYNAMIC EFFECTS OF HYPOTENSIVE DRUGS AND CONSEQUENT DANGERS IN THEIR USE*

B. GOLDBERG, M.D. (RAND), M.R.C.P. (LOND.) and I. R. YUDAKEN, M.B. (RAND), M.R.C.P. (EDIN.)

In recent years a considerable number of drugs have been used in the treatment of hypertension. Their efficacy in reducing the blood pressure varies with the drug or combination of drugs used and from patient to patient. Their ultimate effect on prognosis is not known but in a proportion of patients considerable subjective relief is obtained during treatment and in some an improvement in existing cardiac and vascular disease ensues. However, the lowering of blood pressure may be accompanied by profound readjustments in the circulation through different organs or parts of the body, which in some instances may result not only in unpleasant and harmful but even lethal side effects. A knowledge of the circulatory changes that do occur with these drugs may permit one therefore to anticipate and so perhaps avoid harm resulting from their use.

In this paper some of the haemodynamic effects of the ganglion-blocking agents, of reserpine, and of hydralazine, are presented and discussed with particular reference to the heart and the renal and cerebral circulations. Difficulties encountered in their use are illustrated with case reports, and some of the factors which should be considered in the choice of drugs in the treatment of hypertensive patients are indicated.

Ganglion-Blocking Agents

This group consists of hexamethonium, pentapyrrolodinium (pentolinium, Ansolysen) and mecamylamine (Mevasine) as well as several others. Their action in reducing the blood pressure results from their effect in blocking transmission of impulses through autonomic (sympathetic) ganglia. As far as is known, differences observed between the hypotensive effects of these drugs are in the main due to the rate and completeness of their absorption and excretion and their duration of action. It has been suggested, however, that the hypotension produced by mecamylamine may also be a result of a central cerebral and direct cardiac effect.[1]

When administered parenterally to hypertensive subjects they cause a fall in blood pressure which is usually accompanied by a decrease in cardiac output or, in patients with cardiac failure, by an increase; total peripheral resistance is unchanged or reduced.[2-4] In dogs, ventricular work and coronary blood flow decrease.[5] The decrease in cardiac output results from a reduction in venomotor tone with an increase in the capacity of the venous reservoir.[7] Venous return is reduced and the cardiac output falls. With the reduction in mean arterial pressure and hence coronary filling pressure the coronary blood flow is decreased. Renal blood flow and glomerular filtration rate fall but tend to return within a short while towards control levels even though the blood pressure remains lowered; renal vascular resistance usually increases.[3,6,8,9] These changes may be due to a reduction in cardiac output and a shift of blood away from the splanchnic area to the periphery, where vasodilatation occurs. In both normal and hypertensive individuals with no known cerebrovascular disease there may be no change in cerebral blood flow with moderate falls of blood pressure, or with more marked hypotension the blood flow may be reduced.[10-12] The decrease in cerebral blood flow has been considered to be a passive one, resulting from the decrease in blood pressure rather than from any direct effect on the cerebral arteries.

Smith and Hoobler found that during maintenance therapy with pentolinium a decrease in cardiac output without any significant alteration in total peripheral resistance occurred,[4] although during treatment with a combination of pentolinium

* A paper presented at the South African Medical Congress, Durban, September 1957.

and reserpine no consistent alteration in cardiac outptu was noted.[13] The reduction in blood pressure occurring during treatment has been attributed to this change in

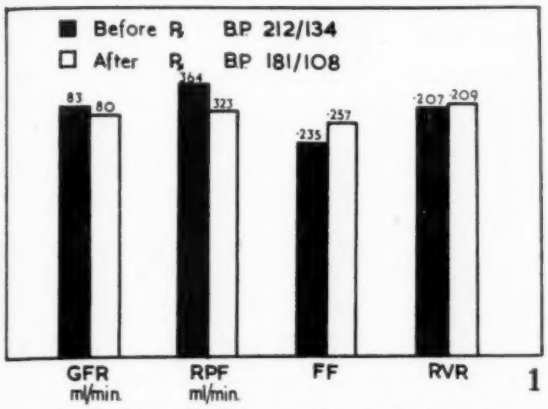

Fig. 1. The effects of treatment with a combination of oral reserpine and mecamylamine on the renal circulation of a hypertensive patient. GFR = glomerular filtration rate. RPF = renal plasma flow. FF = filtration fraction (GFR/RPF). RVR = renal vascular resistance (ratio mean blood pressure/renal blood flow). Numbers on top of columns are absolute values.

cardiac output rather than to any alteration in the peripheral resistance. Maintenance therapy with hexamethonium or a combination of ganglion-blocking drug and reserpine does not result in any marked changes in the renal circulation of recumbent hypertensive patients (Fig. 1) except for a decrease in renal vascular resistance and a slight reduction in glomerular filtration rate.[13,14]

Based on these observations one might expect that renal insufficiency may occur or, when previously present, be aggravated by treatment with a ganglion-blocking drug. That this is so is supported by reports of the development of increasing and fatal uraemia during treatment.[15,16] However, provided renal functional impairment is not too severe and a gradual reduction in blood pressure is achieved, with care these drugs can be used.[13,17,18]

Similarly in the presence of cerebrovascular disease a reduction in blood pressure may be accompanied by undesirable side-effects due to cerebral ischaemia, as illustrated in the following case report:

A 68-year-old man was readmitted to hospital 10 weeks after a previous admission for myocardial infarction. He had had a cerebral thrombosis 18 months previously. On the day of admission he took for the first time some pentolinium pills which had been prescribed for hypertension. An hour or two later he felt faint and collapsed, and on recovering consciousness found his right side to be paralyzed. Examination showed a hemiparesis, blood pressure was 160/90 mm. Hg, and his pupils were widely dilated. During the next few hours the blood pressure gradually rose and eventually averaged 208/123 mm. Hg. Parallel with the rise in blood pressure there was a progressive recovery from the hemiparesis.

Although cardiac output and ventricular work are reduced by ganglion-blocking drugs the coronary blood flow also decreases. This reduction, if proportionately greater than the decrease in ventricular work, may result in myocardial ischaemia.

A 42-year-old man had been observed during a 3-year period during which his blood pressure averaged 210/136 mm. Hg. Because of the development of retinal and electrocardiographic changes he was started on oral reserpine and pentolinium in hospital, and was discharged with an average blood pressure in the recumbent position of about 165/113 mm. Hg. During the next 3 months it became necessary to increase the thrice-a-day dose of pentolinium from 75 mg. to 140 mg. and later to 180 mg. because of the development of tolerance to the drug. When an attempt was then made to increase each dose by a further 20 mg. he developed faintness due to postural hypotension and substernal pain on excretion.

Fig. 2 illustrates ischaemic electrocardiographic changes after the intravenous injection of hexamethonium in a hypertensive patient.

Hydralazine

Hydralazine (Apresoline, 1-hydrazinophthalazine) has been shown to be an effective hypotensive agent acting, both centrally on the brain (possibly the hypothalamus) and peripherally on the arterioles so as to produce vasodilatation and thereby the blood pressure.[15] The injection of hydralazine produces a sympathomimetic effect on the heart, with an increase in heart rate, stroke volume and cardiac output. Vasodilatation occurs, particularly in the splanchnic area and the total peripheral resistance decreases.[19,20] The

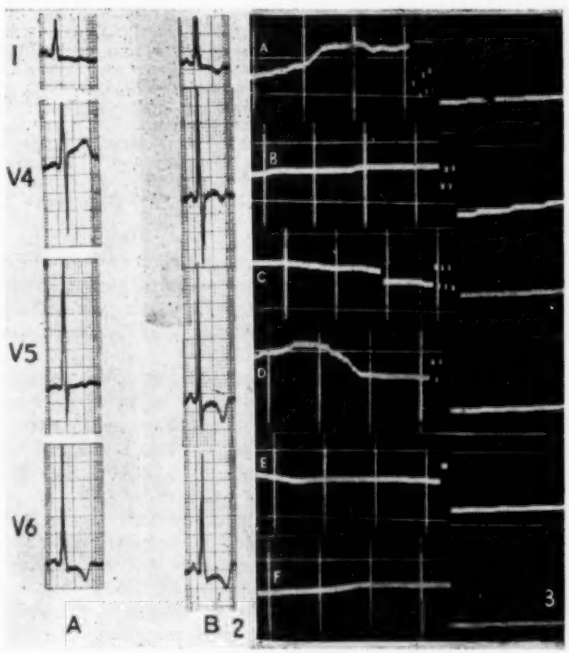

Fig. 2. The effect of intravenous hexamethonium on the electrocardiogram of a hypertensive subject. A: Before injection. B: 20 minutes after injection.

Fig. 3. The effect of intramuscular hydralazine on the digital pulse volume and blood flow of a hypertensive subject. A: Basal. B, C, D, E and F: 15, 30, 45, 60 and 70 minutes after injection. The recordings on the left are at slow paper speed and show a small pulse wave which does not increase after injection. The recordings on the right at fast speed show no significant alteration in the digital blood flow (measured by the steepness of the slope of the curve/unit time).

renal blood flow increases but the glomerular filtration rate is unchanged and the filtration fraction consequently falls.[6,19,21] The digital blood flow may increase or not alter[20,21] (Fig. 3). The cerebral blood flow remains constant in spite of the decrease in blood pressure and the cerebral vascular resistance decreases.[22]

During maintenance therapy with hydralazine the mean resting renal plasma flow is usually not altered significantly, although in individual patients a moderate increase has been noted. Moreover, after a period of treatment oral administration of hydralazine fails to increase the flow significantly, indicating the development of tolerance to the drug.[23]

The effect of hydralazine in increasing ventricular work may be manifest clinically as coronary insufficiency or cardiac failure.

A 50-year-old man had a thoraco-lumbar splanchnicectomy in 1949 because of malignant hypertension. Two years later his blood pressure was about 250/150 mm. Hg and he had symptoms and signs of cardiac failure. He was treated with digitalis, diuretics and for a while with hexamethonium; cardiac failure improved and the blood pressure was reduced moderately. In April 1952 hydralazine was given. On taking 50 mg. *t.i.d.* he experienced for the first time pain in his jaw. On reducing to 25 mg. *t.i.d.* this pain was not felt, but symptoms of cardiac failure returned, with breathlessness and oedema of the legs. This was controlled again with diuretics and hydralazine was stopped for a week. When it was resumed in a dose of 50 mg. *t.i.d.* he had anginal pain about 45 minutes after the second and also the third dose. Hydralazine was again stopped for one day. On resumption pain occurred in the chest, jaw and arms, with palpitations. Thereafter the dose was reduced to 25 mg. *t.i.d.* with no angina but also no significant change in the blood pressure. Hypotensive treatment was stopped for 4 months but when hydralazine was started again angina recurred. Subsequently he was treated with reserpine and hydralazine with a good effect on blood pressure but with the development of severe mental depression.

Reserpine

The mode of action of the rauwolfia alkaloids, of which reserpine is one, appears to be a centrally mediated (possibly hypothalamic) depression of sympathetic nervous activity with resulting peripheral vasodilatation and consequent reduction in blood pressure.[24]

In acute experiments on dogs and in hypertensive patients the intravenous administration of reserpine causes no consistent effect on cardiac output and the fall in blood pressure has been shown to be due to a decrease in peripheral resistance. Similarly no consistent alteration in the glomerular filtration rate or renal blood flow has been observed.[24]

During maintenance therapy with reserpine alone or a combination of reserpine and pentolinium no significant change occurs in the renal plasma flow or glomerular filtration rate. The renal vascular resistance decreases.[9,13,24]

We have observed no deleterious effects due to haemodynamic changes in patients treated with reserpine alone.

Combination of Drugs

Since many patients are treated with combinations of the various hypotensive drugs it is of importance to know whether the action of one is modified by simultaneous treatment with another. It has been shown that pre-treatment with reserpine does not prevent the acute renal haemodynamic changes produced by hexamethonium.[9] Similarly, the effects on renal haemodynamics of maintenance therapy with a combination of reserpine and pentolinium[13] are similar to those reported during treatment with hexamethonium alone.[14] The increase in the heart rate following the administration of hydralazine is prevented if reserpine is also given.[25] It is possible that the action of the ganglion-blocking agents on the cardiac output may be antagonistic to the opposite effect of hydralazine, although hexamethonium does not inhibit the renal vasodilating action of hydralazine.[26] In Table I are summarized the various haemodynamic alterations produced by the individual drugs.

TABLE I. SUMMARY OF THE EFFECTS OF GANGLION BLOCKING DRUGS, HYDRALAZINE AND RESERPINE ON THE CARDIAC OUTPUT AND RENAL AND CEREBRAL CIRCULATIONS

	Ganglion Blockers	*Hydralazine*	*Reserpine*
Cardiac output	−	+	O
Renal blood flow	$\frac{-}{O}$	$\frac{+}{O}$	O
Glomerular filtration rate	$\frac{-}{O}$	O	O
Cerebral blood flow	−	$?\frac{-}{O}$	? O

+ = increase. − = decrease. O = no change. ? = effect doubtful.

DISCUSSION

The heart, kidneys and brain are the important organs which may suffer harm from the haemodynamic changes that occur during treatment with hypotensive agents. The patient who will suffer and the part which will be affected will depend upon the particular drug used and the presence and severity of accompanying vascular disease.

A reduction in blood pressure resulting from the use of ganglion blockers may result in a decreased cerebral blood flow. When cerebro-vascular disease is present, not in the form of hypertensive encephalopathy, but in the form of associated organic cerebral arterial disease, this reduction in blood flow may result in general or local cerebral ischaemia and anoxia. While we have not observed cerebral ischaemia during treatment with hydralazine or reserpine we have seen syncope follow a single injection of hydralazine. In the elderly atherosclerotic hypertensive patient it is likely that a sudden, marked reduction in systemic blood pressure, produced by any means, will result in cerebral ischaemia and its sequelae. It follows, therefore, that in this type of patient hypotensive treatment should be instituted cautiously and only when the disease itself is of sufficient severity to warrant treatment. The aim of therapy is to produce a moderate and gradual lowering of the blood pressure, avoiding sudden sharp reductions. Thereby one may alleviate the symptoms, and perhaps prevent the progression, of the generalized hypertensive vascular disease. The gradual and moderate reduction in pressure that is desirable is characteristic of the action of reserpine, which is the drug of choice in these cases. Treatment with reserpine alone, however, is not always adequate, and then the addition of hydralazine in gradually increasing doses may be effective. Moreover, the postural hypotension which occurs during maintenance treatment with the ganglion-blocking agents is not a problem with reserpine and hydralazine.

In the presence of severe progressive renal functional impairment it is unlikely that the reduction in blood pressure will prevent the usual fatal outcome. However there is little doubt that associated hypertension worsens the prog-

nosis of renal disease, either directly by its effect on the kidneys, or secondarily by the production of cardiac failure. It is important, therefore, in these instances to try and reduce the blood pressure and so retard these changes. When renal disease, although advanced, is static or only slowly progressive it may be possible by treatment to alleviate symptoms due to hypertension and perhaps improve prognosis. Theoretically the drug of choice under these circumstances should be hydralazine, by virtue of its effect in increasing blood flow. We have observed in an occasional individual with severe but only slowly progressive renal insufficiency an apparent improvement in renal function as evidenced by a gradual decrease in the blood urea over a period of months. However, this is unusual and, because it has been shown that hydralazine does not significantly affect renal blood flow during maintenance therapy, the most that can be hoped for in the majority of these cases is that by reducing the blood pressure the incidence of other fatal consequences of hypertension, particularly cerebral haemorrhage and cardiac failure, will be lessened. While hydralazine is the drug of choice when renal disease is severe, it has been shown that the ganglion-blocking agents can be used with care and combined with hydralazine and reserpine in the treatment of these cases. As with patients with cerebro-vascular disease the aim of treatment is to produce a gradual decrease in blood pressure. However, as the ganglion-blocking agents are excreted in the urine, cumulative effects of these drugs may occur unless increments in dosage are small and made slowly. If this is not done, acute hypotension may result, with rapid worsening of renal function due to a decrease in the glomerular filtration rate. In general it is safe to use the ganglion-blocking agents if the blood urea is less than 70 mg.% provided caution is exercised and renal function is checked fairly frequently, particularly by the blood urea. The aim of treatment is to reduce the blood pressure to a level which is not associated with increasing uraemia. If the blood urea does rise it is wiser to allow the pressure to increase slightly by a reduction in the dose or by temporarily stopping the administration of the drug.

We have illustrated the development of angina during treatment with pentolinium; but this is unusual and in the majority of instances the ganglion-blocking agents are the drugs of choice in the treatment of hypertension with associated myocardial or coronary-artery disease. Often symptoms of cardiac failure are improved, as in angina. This results from the decrease in cardiac work. Hydralazine, on the other hand, may increase the severity of the symptoms of coronary insufficiency, or in some instances, as shown, produce them for the first time. It is best to avoid its use in patients with cardiac involvement or to combine it with reserpine or a ganglion-blocking drug if treatment is inadequate without it. The antagonistic effect of reserpine on the tachycardia, and of the ganglion-blocking agents on the increase in cardiac output, produced by hydralazine may prevent or reduce the incidence of side-effects.

No attempt has been made here to discuss the other toxic effects of the hypotensive drugs. Treatment may be difficult because of the parasympathetic blockade resulting from the use of ganglion blockers with consequent genito-urinary, gastro-intestinal and visual disturbances. With hydralazine the production of the drug rash, fever, blood dyscrasia or a collagen-like disease may interfere with treatment. When reserpine is used, in addition to the lesser toxic effects marked mental depression may be produced which may make it necessary to stop the drug. The efficacy of the various drugs in their hypotensive action, and the ease with which control of blood pressure is achieved with a particular drug in in-patients and out-patients has not been discussed. Only the haemodynamic effects have been presented and, although not common, in some patients these changes result in unpleasant symptoms and even harm. It is hoped, however, that a knowledge of the factors discussed will make the treatment of hypertension in the individual patient safer and control easier.

SUMMARY

The haemodynamic effects of a group of hypotensive drugs are discussed with special reference to their effects on the heart and the renal and cerebral circulations. The effects observed in hypertensive subjects of the ganglion-blocking agents and reserpine on the kidney and of hydralazine on the heart are presented and compared. Reference is also made to their effects on the cerebral circulation.

On the basis of these findings possible dangers in the use of these agents in the treatment of hypertension are pointed out and illustrated with case reports. Indications and contra-indications for the use of particular drugs or combinations of drugs in individual patients are discussed.

We are indebted to Dr. M. M. Suzman for permission to study patients under his care and to Prof. H. B. Stein, Department of Clinical Pathology, for providing laboratory facilities.

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The South African Society of Obstetrics and Gynaecologists (Cape Town branch). At the annual general meeting of this society held on 2 June 1958 at Medical School, University of Cape Town, Observatory, Cape, the following committee was elected: Dr. T. St. Vincent Buss (Chairman), Dr. L. J. Abramowitz (Secretary), Dr. P. Massey and Prof. J. N. de Villiers.

PORPHYRIA IN SOUTH AFRICA: THE FAECAL EXCRETION OF PORPHYRIN

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In comparison with the numerous detailed examinations of urine from cases of porphyria relatively little attention has been paid to the excretion of porphyrins in the faeces in these diseases, although it was noted by Gunther (1911) that excessive amounts of porphyrin were present in the stools of chronic and acute cases. Studies by Dobriner (1937), Dobriner, Strain and Localio (1937), Heising (1940), Localio, Schwartz and Gannon (1941) and Nesbitt and Snell (1942) indicated that the normal faecal excretion of coproporphyrin was in the range 200-400 μg. per day; that patients with diseases involving increased haemopoiesis excreted from 2 to 3 times as much; and that excretion by this route was diminished in patients with liver diseases. Dobriner found no evidence of the presence of haemato- or mesoporphyrin in normal or pathological stools.

A few quantitative analyses have been reported on stools from cases of porphyria. Prunty (1946) found 1·33 mg. of coproporphyrin per 100 g. in faeces obtained post-mortem from a case of acute porphyria. Watson (1954) tabulated faecal analyses in 13 cases of the acute intermittent and cutanea tarda types during remission; increased amounts of copro- and protoporphyrin were found. Both these workers recorded finding increased amounts of uroporphyrin in the faeces of their patients. Rimington and his associates [Gray, Rimington and Thomson (1948), Macgregor, Nicholas and Rimington (1952 and Wells and Rimington (1953)] described cases of porphyria cutanea tarda and emphasized the importance of quantitative determination of stool porphyrins in this disorder. They regard high faecal values with normal or only slightly increased urinary values as characteristic of the cutanea tarda form.

Porphyria is common in the White and Bantu races in South Africa and the faecal excretion of porphyrins has been studied in patients and in some of their relations. The clinical manifestations shown by White cases vary even within a single family unit. Cutaneous eruptions and scarring are commonest in males, who rarely suffer episodes of acute porphyria, which occur more frequently in females, in whom the skin lesions are usually milder and often cannot be detected. Both pictures are sometimes demonstrable in the same individual. In family studies occasional members have been found who excrete excessive amounts of porphyrin in their stools but have not shown clinical symptoms—these are regarded as cases of latent porphyria. Porphobilinogen is not increased in the urine of these White patients except in association with symptoms suggestive of an episode of acute porphyria; recent observations show that this is also true of δ-aminolaevulic acid.

Considered individually these patients can be allocated to one or other of the acute intermittent, cutanea tarda or mixed sub-groups of Watson's porphyria hepatica. It is, nevertheless, possible that all these cases are genetically homogeneous, since genealogical studies by Dean (personal communication), based on a number of affected families, indicate a convergence of ancestry to a pair of immigrants from Holland who married in the Cape of Good Hope settlement in 1688. On this basis these South African cases, despite their varied clinical features, would properly belong to one group, which should be differentiated from pure acute intermittent porphyria, in which skin eruptions do not occur.

The Bantu cases of porphyria have already been described elsewhere (Barnes 1955). The great majority of these show skin lesions as the only clinical manifestation of the disorder. Acute porphyria is rare in these people and no case of this type presented during the course of the present study. Confirmation of the clinical diagnosis was readily obtained by the detection of porphyrin in the urine but, as will be shown later, their stool porphyrins were not so markedly increased as those of the White cases and were, in fact, sometimes within normal limits. For this reason it is difficult to fit them into the cutanea tarda group as defined by Rimington.

Our findings on the stools of 4 cases of erythropoietic (congenital) porphyria are also presented in this paper.

Many of the subjects were well and following their ordinary occupations, so that continuous collection of stools to obtain reliable figures for daily excretion, which is the ideal in metabolic experiments, was not practicable and it was decided to analyse casual specimens. As will be seen later, faecal excretion was so markedly increased in many instances that this simplification is justified, but in borderline cases interpretation is difficult. Since the solid content of stools varies considerably, from 4·6 to 38% according to Fowweather (1926), the results were determined in terms of the dry weight of the stools. Ether-soluble porphyrins only were determined by a method eliminating porphyrins derived from chlorophyll and designated coproporphyrin (removed from the ether extract by 0·1 N hydrochloric acid) and protoporphyrin (removed from the ether extract by subsequent shaking with 1·5 N hydrochloric acid). Fuller details are given by Holti *et al.* (1958). It is known that the latter fraction includes the deuteroporphyrin present in the faeces and Watson (personal communication) states that in his experience coproporphyrin, for reasons not immediately apparent, is not always completely removed from the ether extracts of faeces by 0·1 N hydrochloric acid. By his more elaborate procedure results for coproporphyrin in some specimens are higher and for protoporphyrin are lower than by the method used in this study.

RESULTS

Normal Bantu. Stools from 18 Bantu adults convalescing from minor operations or under observation for mild disorders were analysed. These persons were free from signs or symptoms of diseases known to be associated with disturbances of porphyrin metabolism. The results obtained are recorded in Table I. These will be discussed later in relation to the normal range adopted.

TABLE I. PORPHYRINS IN STOOLS OF NORMAL BANTU

	*Coproporphyrin**	*Protoporphyrin**
Minimum	less than 1	less than 1
Maximum	11	37
Mean	7	16

* μg. per g. dry weight.

Adult Porphyrics. These comprised 27 Whites and 19 Bantu. The White subjects were mainly members of the

family described by Dean and Barnes (1955). Many showed active cutaneous eruptions or scars of past lesions and several of the women had had acute episodes. Porphyrins had been detected in the urine of all of them at some time. The Bantu were partly new cases seen currently at clinics and partly old patients who were traced for this study. Skin lesions were not active in all of the latter but an excess of porphyrin was still present in their urine. None of these cases was known to have had acute porphyria.

TABLE II. PORPHYRINS IN STOOLS OF ADULT PORPHYRICS

		White	*Bantu*
No.		27	19
Corproporphyrin*	Min.	23	6
	Max.	800	161
	Mean	242	58
Protoporphyrin*	Min.	103	11
	Max.	1,280	134
	Mean	487	45

* μg. per g. dry weight.

Children of Porphyric Parents. Stools were obtained from White and Bantu children under 20 years of age, one of whose parents was known to be affected. The White families were all of South African stock. We have not yet encountered a family in which both parents were porphyric. The results of porphyrin determinations on the stools of these children are classified in Table III.

TABLE III. PORPHYRINS IN STOOLS OF CHILDREN OF AFFECTED PARENTS

	White			*Bantu*
	Normal	*Doubtful**	*Abnormal*	*Normal†*
No.	21	2	14	13
Coproporphyrin‡				
Min.	0	9	16	1
Max.	14	10	158	11
Mean	7	9·5	52	5
Protoporphyrin‡				
Min.	5	47	51	3
Max.	42	51	212	27
Mean	17	49	116	10

* This group is defined in the discussion.
† All the specimens from Bantu children gave results within normal limits.
‡ μg. per g. dry weight.

Erythropoietic (congenital) Porphyria. Data are available from 4 cases of this rare condition and from some of their relations. A and B are 2 Sudanese siblings (male and female); fuller details are given by Townsend-Coles and Barnes (1957). C is a Bantu female, first reported by Findlay and Barnes (1950), with whom contact has since been maintained. D is a second Bantu female case discovered by Baxter (1958) at the Jane Furse Memorial Hospital in the Eastern Transvaal. Stools from these 4 patients gave the results recorded in Table IV. The parents of A and B and two younger siblings were healthy. Specimens of urine and faeces from these 4 relations, the paternal grandmother and 4 of the mother's 5 brothers were examined and none was found to contain excessive amounts of porphyrin. The father of case C deserted his family soon after the child was born and was never examined. Her mother had no skin lesions, urine has been negative for porphyrins on several occasions, and 2 stools were normal with respect to porphyrin. No excess of these pigments was detected in urine or stool from 2 of the patient's half-brothers. Case D was about 3 years old when the diagnosis was made. Urines and stools from her paternal grandmother, both parents and 4 of her 5 brothers were all normal in porphyrin content.

TABLE IV. STOOL PORPHYRINS IN CASES OF ERYTHROPOIETIC PORPHYRIA

Case	*Coproporphyrin**	*Protoporphyrin**
A	643	79
B	644	17
C	3,000	76
D before splenectomy		
6 specimens	740-1,550	26-113
1 specimen	43	8
after operation		
4 specimens	83-220	29-103

* μg. per g. dry weight.

A complete White family. The diagnosis of porphyria in the adult White subjects referred to above were established on clinical and laboratory findings. Subsequently another family was studied in which every member provided faeces for analysis (Fig. 1).

DISCUSSION

Normal values

Brugsch (1952) determined the copro and non-copro fractions of the ether-soluble porphyrins in stools from a number of healthy subjects, using analytical procedures similar to ours. His non-copro type corresponds to our protoporphyrin. The results were tabulated according to the benzidine test for occult blood given by the specimens; the mean values calculated from his tables are given in Table V. If it is assumed that an average stool contained 80% of water it can be calculated from the over-all means of these groups that the faeces of healthy persons on mixed diet would contain on the average 4·4 μg. of copro- and 11·7 μg. of protoporphyrin per g. dry weight. The upper limits for these pigments in this group were 13 and 37 μg. respectively.

TABLE V. PORPHYRIN CONTENT OF NORMAL STOOLS (BRUGSCH 1952)

Benzidine reaction	*No.*	*Copro type**	*Non-copro type**
Negative	16	104	187
Positive	7†	90	484
Doubtful	13	70	173

* μg. per 100 g. of wet stool.
† One result, much higher than the others, has been excluded.

In a recent investigation of porphyria cutanea tarda Holti, Rimington, Tate and Thomas (1958) regard 20 and 30 μg. per g. dry wt. as the upper limits for copro- and protoporphyrin respectively in the stools of normal English subjects. In this present study 15 and 45 μg. per g. dry wt. have been adopted as the upper normal limits and the results considered doubtful if either pigment exceeded its norm but the total porphyrin was below 75 μg.

The results on the group of 'normal' Bantu subjects on hospital diet fell within these provisional limits, suggesting that there is no marked essential racial difference between these people and Caucasians with respect to porphyrin production and excretion. The diets of the Bantu, however, vary considerably according to their circumstances and the amount of roughage influences the composition of their stools. Analyses by A. R. P. Walker show that the dry solids of faeces, which vary from 15 to 30 g. per day for White South Africans on mixed diet containing white bread,

are from 40 to 60 g. for urban Bantu on a partly europeanized diet and may be as high as 80-100 g. per day for rural Bantu on their primitive diets. Faecal porphyrins of Bantu subjects, expressed in terms of dry stool weight, may thus be low because of dilution by high faecal solids.

Abnormal values in conditions other than porphyria

It is known that stool porphyrin concentration may be influenced by conditions not related to porphyria. Since these must be kept in mind when interpreting results they are here summarized briefly. In blood diseases involving increased haemopoiesis the faecal output of coproporphyrin is increased. The figures given by Brugsch show that the haem ingested on a mixed diet does not affect the copro- but raises the protoporphyrin twofold or threefold. Bleeding in the upper gastro-intestinal tract will have a similar effect; protoporphyrin of 100-120 μg. per g. dry weight has been found in melaena stools. In liver diseases coproporphyrin may be raised in the urine and diminished in the faeces. This is regarded as a diversion of excretion from bile to urine (Watson 1952). Though no example has been encountered it is possible for the stool porphyrin per g. of dry solids to be raised in a person on a small intake of low-residue food, e.g. a faddist or a patient on invalid diet.

Findings in adult porphyrics

The stool porphyrins of all the adult White patients were abnormally high according to the criterion adopted and with one exception protoporphyrin exceeded coproporhyrin. Of the Bantu, 12 showed abnormally raised porphyrin excretion (but at distinctly lower level than the White group), 5 were doubtful, and 2 were within the normal range. In only 7 of these specimens, i.e. less than half, was protoporphyrin greater than coproporphyrin.

The Bantu patients were drawn from an urbanized population and if their stool porphyrin figures are doubled to compensate for dilution by roughage, as suggested by Walker's findings, the means for copro- and protoporphyrin become 116 and 90 μg. respectively, still far below the average values of 242 and 487 μg. found for the White group. The possibility that the difference could be ascribed to a degree of liver dysfunction in the Bantu could only be tested by fully controlled metabolic study of both groups with simultaneous analyses of urine and faeces.

The lower excretion of protoporphyrin relative to coproporphyrin observed in the Bantu patients is so large that it suggests different underlying metabolic disorders in the two groups. That difference in meat consumption is not an important factor is indicated by the similarity of the ratios of these two pigments found in the stools from normal Bantu and European subjects.

Findings in children

About two-fifths of the White children had abnormal stool porphyrins, though none showed clinical manifestations of porphyria. It seems reasonable to regard the children giving abnormal results as latent porphyrics who will become manifest in adult life and pass the affection on to about half of their children. The increases are not as large as those found in the adult group, but it is possible that with increasing age the degree of abnormality will become greater and that more of the children will show this evidence of affection.

No Bantu child showed clinical manifestations of porphyria, all their stool porphyrins were within the normal range, and none showed an excess of copro- over protoporphyrin as did many of the specimens from affected Bantu adults. The ages of these children ranged from infancy to 18 years, and, though the results from 4 of them become abnormal when multiplied by the factor used to compensate for dilution in the adult specimens, we do not know enough about the roughage in their diets to justify this procedure.

The findings in the White children can thus be reconciled with the established inheritance of susceptibility to porphyria in this section of the population. In the Bantu, however, this supporting evidence of heredity was not obtained and the alternative possibility, that the condition may be acquired in these people, remains open.

Findings in erythropoietic porphyria

All the specimens of faeces from this group of patients contained abnormal amounts of coproporphyrin; that from case C indicates how gross the increase can sometimes be in this condition. Protoporphyrin was only slightly raised in some specimens and within normal limits in others. It has been shown elsewhere (Barnes 1957) that, though very unusual, cutaneous lesions may occur in young children in White porphyric families and simulate very closely the picture of erythropoietic porphyria. Determination of the proportion of copro- to protoporphyrin in the stool may thus afford another means of distinguishing between these two forms of the malady.

Whilst case D was under observation before the splenectomy, her urine became very much paler for a few days and one stool analysed during this period contained only 43 μg. of coproporphyrin per g. dry weight. This is a remarkable spontaneous partial remission in a condition in which enhanced excretion of porphyrin is believed to be a constant phenomenon.

No disturbances of porphyrin excretion were disclosed in near relations of these patients by stool analysis.

Detection of latent porphyria

The custom has been adopted of advising patients with porphyria to inform their near relations that doctors should be told of its occurrence in the family. The detection of latent porphyria is very desirable because of the risk these people run of developing acute attacks when treated with certain sedatives, more particularly after surgical operations. To this end the Watson-Schwartz test for porphobilinogen in the urine has proved valuable in other countries but fails in South Africa since porphobilinogen is only found at the time of acute episodes. The findings presented above in White cases and their children suggest that stool examination for porphyrin should be useful in this respect and the results recorded in Fig. 1 on an entire family enable this possibility to be evaluated.

No stool analysis was available for the propositus (II. 6) but his clinical status and the presence of porphyrin and porphobilinogen in his urine shortly before death from a recurrent coronary thrombosis were compatible with an attack of acute porphyria. Characteristic lesions and scars on his hands and forearms indicated that the condition was of the type which is common in South Africa. His mother was alive and well, presenting no clinical features

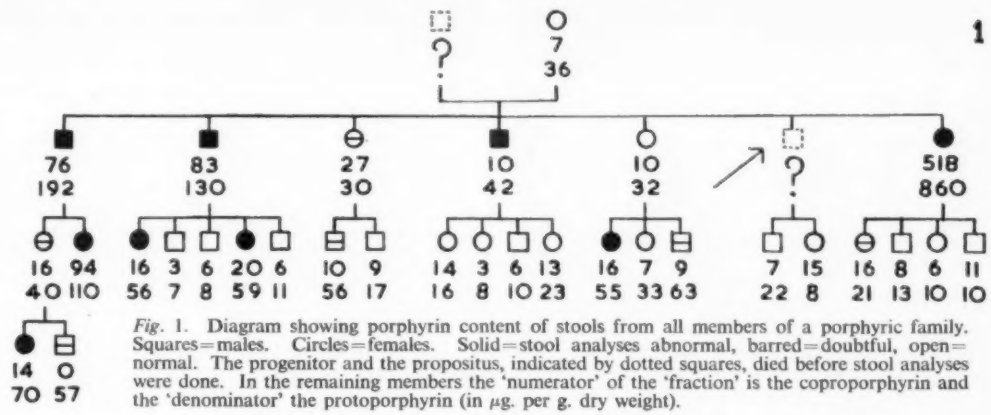

Fig. 1. Diagram showing porphyrin content of stools from all members of a porphyric family. Squares = males. Circles = females. Solid = stool analyses abnormal, barred = doubtful, open = normal. The progenitor and the propositus, indicated by dotted squares, died before stool analyses were done. In the remaining members the 'numerator' of the 'fraction' is the coproporphyrin and the 'denominator' the protoporphyrin (in μg. per g. dry weight).

of porphyria and her stool porphyrins were normal, but his father was a possible link with other affected South African families as he was stated to have had a fragile skin.

Three members of generation II had abnormal stool porphyrins and of these 1 and 7 showed slight scarring as evidence of skin fragility; the third did not, though he was subject to abrasions in his manual work as a fitter. The remaining 5 members who passed abnormal stools were all under 22 years of age and none showed any clinical manifestations. The finding of abnormal stools in some of the progeny of II 1 and II 2 is additional evidence that the two parents are affected. The stool of the eldest child of II 7 was doubtful and those from her 3 younger children were normal. It has already been suggested that the abnormality may be progressive and re-examination of this family in the future may show a different picture.

Stools classified as doubtful were obtained from 6 members, of whom 2 were adults. One of these (II 3) showed a little facial pigmentation but had no lesions and had had two abdominal operations with no complications during convalescence; the other adult and the 4 children presented no signs or symptoms. Interpretation of these doubtful results and, in particular, such groups as II 5 (stool normal) and her 3 children, one of whom fell into each category, requires more knowledge of the variations which may occur in stool porphyrin concentrations.

From these findings it is clear that some near relations of cases of porphyria pass abnormal amounts of porphyrin in their stools though other indications of the disease may be slight or even absent. It would seem wise, in the present state of our knowledge, to regard these people as probably having an inherited susceptibility to the affection. This should be taken into consideration when surgery or treatment with sedative drugs is contemplated.

SUMMARY

1. Copro- and protoporphyrin were determined in the stools of normal Bantu subjects and the findings compared with those reported in normal Europeans.

2. These pigments are increased, sometimes to a very marked degree, in the stools of adult porphyrics in the White population of South Africa. Some of the children of these patients, though free from clinical manifestations of porphyria, also excrete abnormal amounts of porphyrin in their stools. The presence of increased porphyrins in the stools from relations of patients with porphyria is suggestive of latent porphyria.

3. Less marked increases of pigment were found in stools from adult Bantu patients showing cutaneous manifestations of porphyria and the proportion of copro- to protoporphyrin differed from the ratio found in the specimens from White porphyrics. No definite evidence was obtained of increased porphyrins in faeces from children of Bantu porphyrics.

I have to thank the Director of the Institute for facilities to carry out this study. A large proportion of the specimens from the White patients was obtained and sent to me by Dr. G. Dean of Port Elizabeth and access to other patients was granted by many doctors on the Witwatersrand. Fig. 1 was drawn by Miss C. E. Campbell.

The subject matter of this paper was included in a thesis presented by the author to the University of London for the Degree of Doctor of Philosophy.

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EFFECT OF CHLORAMPHENICOL ON THE PRODUCTION OF ANTIBODY TO BACTERIAL AND NON-BACTERIAL ANTIGENS

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One of the fundamental problems associated with the use of antibiotics in acute infectious disease states is the effect which the antibiotic may exert on the humoral response of the host to the causative organism. Depression of antibody response in this way is often quoted as one of the dangers of antibiotic therapy. Theoretically, there is an expectation that the reduction in the amount of antigen available for antibody response that is brought about by depression of multiplication of the infecting agent would lead to a diminution in the amount of antibody compared with non-treated hosts where multiplication of the causative agent is not so inhibited. Various types of host-parasite-antibiotic relationship have been investigated in an attempt to assess the effect of antibiotics on antibody production. No clear-cut pattern of response has emerged from these studies. Conflicting results have been reported which appear to depend on the type of antibiotic used, the nature of the infecting agent, and a number of variable host factors.

Our interest in this problem was aroused by the observation that the incidence of the relapse phase in typhoid fever may be considerably increased by inadequately prolonged treatment with chloramphenicol, as compared with non-treated patients or with those given an adequate course of the drug. This finding has been reported by a number of authors (El Ramli, 1950 and 1953; Smadel *et al.*, 1949). It has usually been suggested that the increased incidence of the relapse phase is secondary to a depression of antibody response as a direct result of the reduction in the amount of antigenic stimulus available. We have questioned this view, however, since in our experience the relapse phase in typhoid fever occurs late in the disease at a time when levels of agglutinating antibody may be very high (Watson, 1957). We have observed these high antibody titres in spite of the fact that the patients have been treated with chloramphenicol.

The present investigation was undertaken to try to determine the effect of chloramphenicol on the production of agglutinating antibody to bacterial antigens and on the production of Forssman-type antibody.

MATERIALS AND METHODS

Bacterial Strains and Immunization Procedures

The following strains were used to demonstrate antibody production against somatic, envelope and flagellar antigens respectively: (a) *Salmonella typhi* (0.901 strain, N.C.T.C. 5759), (b) *Escherichia coli* (5396/38 strain, which is a potent source of Vi antigen), and (c) *Salmonella typhi-murium* (N.C.T.C. 5710).

All strains were subcultured daily in heart-digest broth for 10 days before use. Suspensions for immunization were prepared by subculturing onto nutrient agar slopes, incubating for 18 hours at 37·0°C and then harvesting in sterile 0·85% saline. An alcoholized suspension of the *S. typhi* strain and a formalinized suspension of the *S. typhi-murium* strain were prepared in the usual way. The Vi-containing *E. coli* strain was not killed. All suspensions were standardized to contain approximately 20×10^8 organisms per ml. by means of opacity tubes.

Healthy adult rabbits of approximately 3,500 g. weight were injected intravenously on alternate days with a dose of 0·2 ml. of bacterial suspension for 4 injections, followed by a further 2 injections of 0·4 ml. each, in the case of the *S. typhi* and *S. typhi-murium* suspensions. In the case of the *E. coli* suspension the same doses were given, preceded by an initial intravenous injection of 0·01 ml. Six rabbits were used for each suspension. Chloramphenicol was given concurrently to 50% of the rabbits in each group by daily intramuscular injection in a dose of 25 mg. per lb. of body weight. Antibiotic injections were discontinued the day after the last immunizing injections. All rabbits were bled on the 10th day after the last injection and antibody titres were estimated.

Non-bacterial Antigen

The effect of chloramphenicol on the production of antibody to a non-bacterial antigen of the Forssman type was investigated.

Two kidneys from a freshly killed guinea pig were emulsified in 25 ml. of sterile saline in a blender. The suspension was incubated at 37·0°C for 4 hours and then kept in the cold overnight at 4·0°C. It was then centrifuged at 2,000 revs. per minute for 5 minutes to deposit gross particles. The supernatant suspension was removed and injected intravenously in 0·5 ml. amounts into each of 6 rabbits. Further intravenous injections of 1·0 ml. were given on the 4th, 7th and 10th days. Preliminary Forssman antibody titres were estimated on the rabbit sera before the injections were begun. Chloramphenicol was given intramuscularly to 3 of the rabbits as described above. Trial bleeds were performed on the 10th day after the last injection.

Antibody Titrations

Antibacterial agglutinating antibody was titrated with fresh saline suspensions of living bacteria washed from 18-hour agar slope cultures (Felix and Pitt, 1934). Serial dilutions of the sera were incubated with the suspensions for 2 hours at 37·0°C in 3 by ½ inch tubes. The tubes were then stood at room temperature for a further 24 hours before reading.

Forssman antibody was titrated with serial doubling dilutions of serum in 0·5 ml. amounts. Aliquot volumes of a 2·0% suspension of thrice-washed sheep erythrocytes suspended in 0·85% saline were added together with an excess of complement. Tubes were incubated at 37·0°C for 4 hours and the end point was taken as the last tube showing clear sparkling haemolysis.

RESULTS

(a) *Effect of chloramphenicol on antibody response to bacterial antigens*

In Table I are detailed the titres obtained from different rabbits immunized with the varying antigens. The figures show that in no case is there evidence of a reduction in the amount of antibody produced by the rabbits which received

TABLE I. EFFECT OF CHLORAMPHENICOL ON THE PRODUCTION OF ANTIBODY TO VARYING BACTERIAL ANTIGENS

Type of antibody	*Serum agglutinating titres (reciprocal values)*	
	With chloramphenicol	*Without chloramphenicol*
'O' antibody	Rabbit (1)—10,240 Rabbit (2)— 5,120 Rabbit (3)— 5,120	Rabbit (4)—10,240 Rabbit (5)— 5,120 Rabbit (6)— 5,120
Vi antibody	Rabbit (1)— 5,120 Rabbit (2)— 5,120 Rabbit (3)— 5,120	Rabbit (4)— 5,120 Rabbit (5)— 5,120 Rabbit (6)—10,240
'H' antibody	Rabbit (1)— 1,280 Rabbit (2)— 1,280 Rabbit (3)— 1,280	Rabbit (4)— 640 Rabbit (5)— 1,280 Rabbit (6)— 1,280

supplements of chloramphenicol under the experimental conditions described. We are concerned here with final titres after a full course of immunization and not with the rate of antibody production. It is possible that chloramphenicol may have an effect in delaying the production of antibody, as compared with non-treated animals, but without affecting the final titres. It is, for example, our impression that patients with typhoid fever treated with chloramphenicol in the first few days of illness exhibit a delay in antibody production. Similarly, Smadel (1954) has shown that antibody production in human infections with *Rickettsia orientalis* is delayed by early chloramphenicol therapy.

(b) *Effect of chloramphenicol on production of antibody to non-bacterial antigen*

Table II shows the response to heterophile-type Forssman antigen in the two groups of experimental animals. Here again there appears to be no difference in the response of the two groups, the titre differences varying by only one tube. The dosage of chloramphenicol employed in both investigations is comparable to that used in human infections. The findings would also indicate that chloramphenicol in these dosages has little if any effect on the antibody-forming reticulo-endothelial cells. It is known, however, that large doses of antibiotics may exert a toxic effect on reticulo-endothelial tissues.

TABLE II. EFFECT OF CHLORAMPHENICOL ON THE PRODUCTION OF ANTIBODY TO FORSSMAN-TYPE ANTIGEN

Titres after immunization

With chloramphenicol	*Without chloramphenicol*
Rabbit (1)—1,280 (16)	Rabbit (4)—2,560 (32)
Rabbit (2)—1,280 (16)	Rabbit (5)—1,280 (16)
Rabbit (3)—1,280 (8)	Rabbit (6)—1,280 (16)

Reciprocal values of preliminary titres before immunization are shown in parentheses

DISCUSSION

The findings reported here regarding the effect of chloramphenicol on the production of antibody to non-bacterial antigen are essentially in agreement with most previous reports on the subject. Giunchi *et al.* (1953), for example, studied the action of penicillin, streptomycin, chloramphenicol, oxytetracycline and chlortetracycline on the production of haemagglutinins in rats injected with group-0 Rh-negative human erythrocytes. The antibody titres in these animals did not differ significantly from the contol group. Such results might be expected on *a priori* grounds if the antibiotic agents are not given in doses which will depress reticulo-endothelial cell function. One of the few reports describing a diminution of antibody production to non-bacterial antigen is that of Stevens (1953) using radio-iodinated bovine gamma globulin.

With bacterial antigens, however, the situation is less clear, certain reports indicating an apparent diminution in antibody produced by antibiotic-treated animals, as compared to control groups. Other workers, however, have been unable to confirm these findings. Ceccarini (1947) found that penicillin had an unfavourable effect on agglutinin production against *S.typhi* in man, and De Marchi *et al.* (1949) reported similar observations in the rabbit. Green *et al.* (1951) on the other hand found no difference in agglutinin titres in patients given TAB vaccine with or without penicillin. Similarly, Ferrata and Olivari (1950) reported that chloramphenicol had no effect on antibody production against *S.typhi* in rabbits. Other reports with chloramphenicol and *S.typhi* in different types of experimental animal seem to support these findings.

The reasons for these conflicting observations are uncertain. Variations in the type of antibiotic, the type of infecting agent and host factors may all play a part singly or in combination. With regard to host factors some interesting findings relating to the effect of diet have been reported. Slanetz (1953), for instance, found that when rats and mice were fed on a diet supplemented with either chlortetracycline or oxytetracycline for a short period, there was an increase in antibody production against *S.enteritidis*. When, however, these supplements were added for a long-term period, there was a depression of antibody response. Such depression could be counteracted by the addition of thiamine or yeast to the diet. Stevens (1953) measured the rate of antigen disappearance in rabbits as an indication of antibody response, using radio-iodinated bovine gamma globulin as antigen. He found that oxytetracycline, chlortetracycline, penicillin and dihydrostreptomycin all produced a marked delay in antigen removal. The response, however, was not constant, and was not observed at all in certain rabbits. Stevens also found that X-irradiation or restriction of the protein content of the diet produced a more marked effect than antibiotics in delaying antigen removal. The mode of action of antibiotic in diminishing antibody production in dietary-restricted animals is problematical and it is not at all certain that this is necessarily a constant effect. It may be that there is a failure of protein absorption from the gut. On the other hand, the action of certain antibiotics such as penicillin appears to result in a failure of protein synthesis. It has been suggested, for example, that penicillin interferes with certain enzyme systems such as ribonuclease and galactosidase. It may be, then, that the antibiotic effect is exerted at a cellular level and that a reduction of antibody formation is aggravated by a lack of 'building blocks' which results from protein deficiency. Edsall (1955) has pointed out the difficulty in translating these results to the situation which exists within the human host. Our own experience, however, in a non-European community where the average protein intake is low, does not suggest that antibody formation, at least in the case of antibody against *S.typhi* is less than that found in better-fed communities.

Some attention has also been given to the production of antitoxin in the presence of antibiotics. One of the few reports is that of Ramon *et al.* (1951), who found no differences in antibody titres to staphylococcal toxoid in penicillin- or streptomycin-treated animals as compared with control animals.

One important aspect of this problem has received little consideration, namely, whether antibiotic agents may result in qualitative changes in the type of antibody produced. This may be a factor of some importance for, if antigenic changes resulted from antibiotic therapy, they might lead to the production of antibody which does not possess the protective power of the normal-type antibody. Servant (1951), for example, has shown that treatment of certain strains of *S.typhi* and *E.coli* with dihydrostreptomycin may lead to a decrease in the amount of extractable polysaccharide of as much as 300% compared with the non-treated organisms. Similarly

Farhi and Lamensans (1956) found that strains of *S.typhi* adapted to grow in chloramphenicol at a concentration of 3.0 μg per ml. became less susceptible to agglutination by anti-Vi sera and more susceptible to agglutination with anti-'O' sera. They also found that the antibodies produced in response to chloramphenicol-modified organisms were less protective than those produced against the parent strains. This problem is at present under investigation in our laboratory.

SUMMARY

Under the experimental conditions described it was not possible to demonstrate any quantitative effect on antibody production as a result of administration of chloramphenicol to rabbits. Antibody production was measured against the following bacterial antigens, (a) Vi antigen (*E.coli* strain), (b) 'O' antigen (*S.typhi* 0.901), and (c) 'H' antigen (*S.typhi-murium*).

Similarly no depression of antibody production against Forssman-type antigen (guinea-pig kidney) was detected.

It is suggested, however, that antibiotic agents may lead to a qualitative change in antibody due to alteration of antigenic structure in the case of bacterial antigens.

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CARDIAC REVASCULARIZATION IN CORONARY ARTERY DISEASE

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Coronary arteriosclerosis, with its resulting myocardial ischemia,* was first recognized by Morgagni in 1707 and was vividly described by him in 1761.[19] Today, coronary insufficiency is responsible for more than 75% of all heart disease, and in the United States alone approximately 800,000 new cases of myocardial infarction occur annually. Of these, about 320,000 patients die. Affecting man in his prime, coronary insufficiency has become the number-one problem of disability in the population as a whole and in the medical profession in particular. Until recently, its solution remained entirely in the hands of the internist, who continues to maintain a deeply entrenched attitude similar to that he held toward the the problem of mitral stenosis some 10 years ago. Since, however, medical treatment has been of little avail, a new approach seems warranted. It is possible that surgical intervention may provide some hope for victims of this disease. Obviously, prevention is to be desired, but when this has failed, the direct approach to the study of coronary artery disease is the most effective. Toward this end, established experimental facts should be applied to the clinical problem.

A thorough knowledge of the anatomic, pathologic, and physiologic phenomena associated with the coronary arteries is essential. The coronary arteries arise from the anterolateral sinuses of Valsalva of the aorta, the right coronary artery passing laterally in the sulcus between the right auricle and ventricle. It divides into a posterior descending branch, which supplies the major portion of the posterior surface of the heart and the interventricular septum, and a smaller branch, which anastomoses with the circumflex branch of the left coronary artery. The left coronary artery passes behind the pulmonary artery to reach the anterior surface of the heart; immediately below the left auricle, it divides into the circumflex and anterior descending arteries. The anterior descending branch passes downward in the interventricular sulcus to the apex, whereas the circumflex branch swings around the base of the left atrium almost as far as the posterior sulcus to reach the apex of the heart. The coronary veins course parallel to the branches of the coronary arteries, returning the blood to the right atrium by way of the coronary sinus. The tributaries of the veins, however, consist of a far richer interlocking system than the arteries; they are far more numerous and have more communications. This anatomic arrangement is of utmost importance in the consideration of some operative technics designed to improve the supply of blood to the myocardium. The myocardium is richly supplied with vascular channels, the capillaries coursing along the cardiac muscle fibers.

One peculiarity of the circulation that deserves particular mention is that the coronary arteries behave as end arteries, with little or no intercoronary communication in about 90% of hearts. Minute anastomoses exist, however, which are capable of gradual enlargement and development. Other peculiarities of this circulation are the presence of direct channels from the arterioles, from the capillary bed, and from the coronary veins directly into the cardiac lumen—the Thebesian veins and arterioluminal vessels. Deep in the myocardium, in addition to the capillary bed, are thin-walled irregular channels known as myocardial sinusoids.

Mechanisms of myocardial nutrition exist other than through the coronary arterial system; for example, an extensive system of vascular communication between the lumina of the cardiac chambers and the myocardial capillary bed forms an important nutritional route in fishes and some amphibia, in which coronary arteries may be small or absent. Although it does not contribute significantly to adult human myocardial nutrition, it must be helpful in maintaining life in the presence of complete coronary occlusion. Another source of myocardial nourishment is the myriad of minute vessels at the junction of the visceral and parietal pericardial reflection. These vessels, arising from intercostal, mediastinal, esophageal, and bronchial arteries, are largely responsible for the new capillary vascularity that develops

*American spelling retained throughout.

in the presence of adhesions secondary to pericardial and epicardial irritation. Anastomoses between these capillary beds and the myocardial capillary bed have been demonstrated.

Actual obstruction to coronary arterial flow consists in atherosclerotic thickening or formation of a plaque within the first few centimetres of the coronary arteries. The end result of this sclerosis is modified by a number of factors: anatomic structure of the coronary vascular system, arterial head pressure, venous back pressure, collateral circulation, and natural response to gradual occlusion of the coronary flow of blood.

CARDIAC REVASCULARIZATION

Pre-eminent in the development of a surgical approach to sclerosis is Claude Beck,[5-8] who, in his many years of animal experimentation in more than 6,000 dogs, has classified death from coronary disease into two types, both related to blood supply, but otherwise different. In the first type, the heart is electrically unstable, associated with trigger zones in localized areas of ischemia, with little destruction of muscle. A deficiency of oxygen in the dry area often produces arrythmia and fatal ventricular fibrillation. Increased flow of oxygenated blood to such an area will result in a more stable heart. In the second type of death from coronary disease, an appreciable amount of muscle has been destroyed in an electrically stable heart. Nothing can be done to revive destroyed muscle and replace it extensively by fibrous connective tissue. The myocardium largely gives way, and heart failure ensues.

Most deaths from coronary disease fall into the first of these groups, in which unequal oxygenation of the myocardium exists. These trigger zones, or ischemic dry areas of myocardium, become ectopic centers for impulses and, in turn, disrupt the co-ordinated mechanism of the heart beat. The destructive property of a trigger zone can be reduced by as small a quantity of blood as 1-5 cc. Beck[7] has pointed out, after the observations of Zoll and associates,[25, 26] that normal intercoronary arterial communications exist in only about 9% of normal human hearts; if the coronary arteries become occluded slowly, about 58% of these hearts will exhibit some intercoronary communication, When occlusion is complete, the incidence rises to 89% for acute closures and 100% for insidious closures. The presence of these intercoronary anastomoses makes maintenance of life possible despite the presence of almost complete or even complete occlusive disease. 90% of all deaths from coronary disease are caused by lack of natural intercoronary communication.

Methods of overdevelopment of these intercoronary vascular channels, artificially or naturally, may prevent necrosis of the myocardium when the supply of blood from the main source has been curtailed. Expansion of intercoronary communications, with increasing flow of oxygenated blood, can impede the development of electrical instability.

Increase of Supply of Blood

Methods of increasing the supply of blood to the myocardium have followed various patterns, largely as a result of the efforts of the pioneers, Claude Beck[5-8] and Lawrence O'Shaughnessy and associates.[21, 22] They have, in general, been directed toward (1) more complete and more uniform distribution of blood in the coronary system, (2) increase in supply of blood from external sources, and (3) resection or correction of occluded segments of the arteries with restoration of the channel. Like many of the significant developments in vascular surgery, revascularization of the myocardium originated in the laboratories of the Frenchmen, Leriche and Fontaine,[17] in 1932. These investigators implanted the pectoralis muscle into the myocardium and significantly reduced the fatality rate in dogs on ligating the descending branch of the left coronary artery. Lezius[18] modified this approach somewhat by attaching the lung to the myocardium; his animals were also able to survive ligation of the left coronary artery. Beck,[5] in 1932, promoted vascular adhesions by suturing the pectoralis minor muscle to the myocardium, and O'Shaughnessy,[21] who used the great omentum for the same purpose, established a collateral extracardiac circulation, with significant relief of pain, in about 30 patients. His project was terminated by his death at Dunkirk, and little further clinical work in this field was published for many years. Heinbecker and Boston,[15] in 1939, produced irritative pericarditis by intrapericardial injection of carborundum sand and sodium morrhuate. In 1940, Fauteaux[12] ligated the great cardiac vein in dogs on the premise that mechanical distention of the direct arteriovenous communication improved survival of tissue after arterial occlusion. Thompson and Raisbeck,[23] in 1942, applied Heinbecker's method in human patients but substituted talc and asbestos for the sand and were successful in promoting collateral extracardiac circulation.

In 1955, an entirely new approach was demonstrated by Vineberg and associates,[24] who implanted the internal mammary artery into a myocardial tunnel. Experimentally, at least, some branching and budding from the terminal end of an open intercostal branch ensued in the ischemic heart. These new branches, joining with existing myocardial arterial channels, assured flow from the extracardiac source. Lung, pedicled skin graft, and pedicled jejunal graft[16] have all been used to increase the supply of blood to the myocardium from external sources. Most of these, however, provide only superficial revascularization. Recently, again largely as a result of Beck's vast experience, efforts to increase the effective flow of blood through the myocardial bed have been focussed on stimulating overdevelopment of the intercoronary collateral circulation. Flow of blood from the descending aorta, by way of a vascular graft, to the coronary sinus, which is later incompletely ligated, is the essence of the Beck II procedure. Although studies by Bakst and associates[3] have demonstrated gradual occlusion of the graft, with abolishment of flow, within 3-6 months after implantation, tremendous overdevelopment of the intercoronary collateral circulation has been stimulated before the cessation of flow within the graft. Ligation of the coronary sinus alters the venous back pressure, and this chronic passive congestion, in itself, leads to some overdevelopment of the intercoronary system.

The Beck I procedure, simpler and apparently just as effective, consists in replacing the more complicated aorta-coronary sinus graft. This operation has 4 component manoeuvres, viz. (1) mechanical abrasion of the lining of the parietal pericardium and surface of the heart, (2) application of 0.2 g. of powdered asbestos, (3) partial occlusion of the coronary sinus to a diameter of about 3 mm., and (4) grafting of the parietal pericardium and mediastinal fat to the surface of the abraded heart. Each part achieves some beneficial effect. Intercoronary channels are stimulated and developed,

the oxygen differential is reduced, and some additional extracardiac blood is brought to the heart.

An important question concerns the quantity of extra blood needed by an ischemic heart. Only a few cubic centimeters per minute may be needed in the presence of an occluded coronary artery. 5 c.c. per minute, or approximately 300 c.c. per hour, will carry a dog through the crisis of occlusion of the descending coronary artery. Even if an infarct occurs, life will be maintained. The Beck operation permits the coronary artery to be perfused with at least 280 c.c. of blood per hour; this reduces oxygen differential and preserves viability of cardiac muscle. Since death from coronary occlusion results from iniquities in supply of blood to contiguous areas of the myocardium, which lead to oxygen differential, electrical instability and ventricular fibrillation, redistribution of a few c.c. of available blood to the appropriate site by this operative procedure can prevent the catastrophic sequelae of coronary artery disease.

Harken and associates[14] used a simple procedure in at least 20 patients, in whom areas of the epicardium had been removed chemically with a 95% solution of phenol. The lingula pulmonis was then attached to the denuded myocardium. An irritative effect was added to the procedure by application of powdered asbestos and talc. Whereas this method is yet another of primary superficial revascularization, it emphasizes the importance of removal of the epicardial barrier in permitting the development of anastomosis from the coronary collateral to the extrinsic collateral circulation. Other new surgical possibilities have included (1) replacement of diseased segment of coronary arteries by a graft, (2) endarterectomy of coronary vessels,[1, 2] and (3) grafting from a systemic vessel to a coronary artery beyond the point of occlusion. Since the basic problem is, obviously, one of diminished supply of blood to the functioning myocardium, successful removal of the occluding plaques or replacement of the occluded area is a more direct and appealing approach. Experimental work along these lines is in progress throughout this country and with utilization of the cardiac bypass, may perhaps lead to clinical application. Murray,[20] a few years ago, reported perfusion of the distal portion of an occluded segment of the anterior descending artery during its resection and replacement by a graft.

The most recent approach to the problem of myocardial revascularization has been devised by Glover,[13] who, following the teaching of some Italian surgeons, has advocated simple ligation of the internal mammary arteries. This permits shunting of blood into the pericardiacophrenic artery, with increased flow of blood to the pericardium and epicardium and, consequently, to the myocardium. This simple procedure, frequently possible under local anesthesia in patients who are extremely ill soon after myocardial infarction, has resulted in dramatic relief of pain in over 90% of 100 patients operated upon by Glover. Sixty-six of 70 patients originally operated upon by the Italian workers, Battezzati, Tagliaferro, and De Marchi,[4] of Genoa and Parma, became free of pain. This relatively innocuous procedure may hold great promise, but basic experimental work has yet to be published, and further experimental and clinical reports may be expected in the near future.

Criteria for Selection of Patients

In Beck's opinion, the most desirable patient is one who has had disease of the coronary artery for one or more years, has had one or more infarcts, is still ambulatory and can do some work, is lean rather than obese, and has coronary pain.[7] If an infarct has occurred, 6 months must elapse before operation is undertaken, to allow some natural development of intercoronary channels. Contrary to expectation, the risk is greater in young persons, in whom the process is much more rapid and malignant. The large failing heart constitutes an unequivocal contra-indication to operation, and patients with extensive destruction of muscle obviously cannot be benefited by surgical intervention. Also hazardous is the presence of progressively severe angina without demonstrable infarction, since in such patients areas of ischemia may develop during or immediately after operation.

Operation should never be considered as a salvage procedure to be applied when medical treatment has failed. In persons of about 50 years of age who have mild to moderate anginal pain on effort and one or more infarcts, the operative fatality rate is about 3%. In those who have more advanced disease, with moderate to severe angina pectoris and one or more infarcts, the operative fatality rate is about 5%. In patients with severe coronary disease, or 'salvage' cases, it rises above 25%. Effective treatment of coronary arterial insufficiency must (1) prolong life, (2) reduce invalidism and disability, (3) maintain productivity and well-being, (4) relieve pain and discomfort, and (5) be accompanied by a non-prohibitive operative risk.

Results and Evaluation of Operation: Beck Procedure

On the basis of collective reports of over 200 patients evaluated 6-12 months after operation, Beck has reported that 45% obtain complete relief from pain and 45% experience diminution of pain; 35% are able to return to work without limitation of activity, whereas 55% can return to work with some restriction of duties. In Brofman's series of 75 patients,[10, 11] 44 have been followed up 10-30 months after operation. Only 2 have died of the disease; 27, including coal miners, laborers and medical practitioners, have returned to full-time work; 10 are working more than before operation, and 4 are still unable to work at all. The safety and effectiveness of the procedure in producing more adequate distribution of coronary blood flow seems beyond question. Occlusion will undoubtedly continue to occur, since no means of preventing this disease has yet been found, but the operation appears to lessen the effects of occlusion when it does occur. It cannot, however, revive degenerated myocardium, and if the occlusive disease progresses very rapidly, it may overtake the benefit derived from the operation.

SUMMARY AND CONCLUSIONS

Recently, increasing interest has been directed toward the surgical treatment of coronary insufficiency, one of the most important medical problems confronting us today. Various methods have been proposed for increasing the diminished supply of blood to the myocardium in coronary sclerosis, all aimed at greater and more uniform distribution of blood to the myocardium and resection of occluded arterial segments with re-establishment of the channel. Effective surgical treatment must prolong life, reduce disability, maintain well-being, relieve pain, and involve a non-prohibitive risk. The Beck II operation appears to be safe and effective. Other procedures for cardiac revascularization have been advocated, and additional ones are being continually devised. Most recent of these is ligation of the internal mammary

artery, but sufficient time has not yet elapsed for definitive evaluation. Experimental and clinical evidences warrant more widespread use of surgical treatment in selected patients with coronary artery disease.

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THE SINGLE-DOSE TREATMENT OF OXYURIASIS WITH PROMETHAZINE HYDROCHLORIDE: A CAUTIONARY TALE

THEODORE JAMES, *Pinelands, Cape of Good Hope*

The modern methods of treating threadworm infestation are rather tedious. To administer doses of a medicament more than once a day for at least 7 days in succession, and to repeat the course of treatment after a 7-10 day interval requires a degree of persistence and patience which is not always forthcoming; nor, in many cases, does it appear worth while in view of the great probability of reinfestation. A single-dose method of treatment for this annoying and potentially harmful complaint will be eagerly welcomed. For this reason I followed to the original article a recent advertisement drawing attention to successful work by Avery[1] along this line, and on this credential, which appeared wholly convincing, I decided to try the single-dose treatment he described, when the next occasions arose.

Avery records that he achieved eradication of the threadworm in 97 of his 100 cases, ranging from 3 years of age to mature adults, after one oral dose of promethazine hydrochloride *B. P.* He used the Wyeth product but the identical substance is also produced by Rhone-Poulenc and May and Baker. Avery's method is to administer 125 mg. of promethazine hydrochloride at bedtime. He advises no preliminary preparation and the dose is the same *irrespective of the patient's age*. He found this treatment to be rapid, effective, non-toxic and inexpensive.

Promethazine is a derivative of phenothiazine, which has been used intermittently for the treatment of vermiculous patients since 1940 and is not without unpleasant side-effects. Promethazine hydrochloride is N-(2′-dimethylamino-2′-methyl) ethyl-phenothiazine hydrochloride. It is much used in clinical practice as an antihistaminic, and has a marked anti-adrenaline effect, a noticeable hypnotic influence, a slight atropine-like action but a strong antiemetic quality. It has also some local analgesic action. Given at bedtime it should induce restful sleep. Makers of the drug recommend a dosage of 15-25 mg. per day in a single dose for adults or in divided doses for children of 5-10 years of age. It appears to be well tolerated in this range of dosage but side-effects observed in some patients have been gastric upset, somnolence, dizziness, slight disorientation, slight headache and visual disturbances, pains in limbs and joints, and ataxia.

Such side-effects as the foregoing were allowed for, but undue regard was not paid to an incidental comment by Avery on his results 'that 5% of children 4-10 years old experienced nightmares on the night of medication, which it is suggested may represent the toxic by-products of heavy infestation released by the activity of the drug upon the worms'. Sisbe[2] lists nightmares as the third most common manifestation of threadworm infestation.

THE TALE

The whole of the W. family, parents and 2 daughters aged 4 years and 6 years were judged from the symptoms to be fairly heavily infested with threadworms, and they agreed to try the single-dose method of treatment rather than the longer piperazine course.

At 5.30 in the evening the two children were each given 125 mg. of promethazine hydrochloride by mouth. At 8.30 p.m. the nursemaid noticed that the younger child was unusually restless in her sleep, and soon after the child began to talk nonsense, with slurred speech, and seemed to be in a state between waking and sleeping. At 10.30 p.m. I was called because the parents returning home were alarmed by the child's rather gross incoordinate and ataxic movements of the whole body. When I saw her she was agitated and thrashed about intermittently, attempted to climb, unsteadily, out of the bed. She accompanied these bodily movements with a continuous, nonsensical, slurred commentary on what were hypnagogic hallucinations. She appeared repeatedly to fall asleep only immediately to startle awake. There were times when she seemed to understand words addressed to her and yet showed no recognition of her parents. There was a picking at the bedclothes, sudden piercing screams, frequent giggling and often a belligerent attitude to whomever happened to be close to her. Her pupils were moderately dilated in the ordinary electric lighting. The deep tendon reflexes were not exaggerated nor depressed and were equal bilaterally. This distressing behaviour immediately raised the disturbing question of acute poisoning by the promethazine. At 1.30 a.m. the child vomited a quantity of the preceding day's food whereupon she was given milk with a quick-acting barbiturate, which she promptly also vomited. At 2.30 she was quieter, at 4.30 she appeared to sleep, and at 6 a.m. she was 'dead to the world'.

At 1.30 a.m. the elder sister began to manifest identical psychical disturbances and followed her younger sister's pattern in all its detail. An attempt was made to sedate her with 'Nepenthe' from the beginning but by 4.30 a.m. she was wide-eyed and hallucinatory. Barbiturate was given her at this time and by 5.30 a.m. she, too, fell asleep.

Both children awoke at 6 p.m., 24 hours after the promethazine had been swallowed. Sleep had been deep and their appetite on wakening was ravenous.

This 'sleep-disturbance' having ended so happily it was discussed with the parents in the light of day and it was apparently satisfactorily explained away by Avery's surmise of toxic by-products of heavy infestation liberated by the action of the drug. When it was added that not one of the 5% of Avery's cases that had suffered 'sleep-disturbances' had been older than 11 years, the father *volunteered* to submit himself to this single-dose method of treatment—he was so horrified by the thought that he harboured the worms in his own body—and took a 125 mg. dose of promethazine. He was a man of 35 years weighing 200 lbs. and over 6 feet tall. I was *not* called in that night to witness, by all accounts, another remarkable manifestation of cortical disorientation in this big man. But the description given to me by his wife was only credible because of my own experiences with his daughters. He too, awoke or seemed to awake from a restless sleep into a strange bellicose nightmare, unmanageable by his wife. He spoke strangely, acted in a queer manner, and at times became vicious and destructive. This behaviour continued until sunrise when he fell into a deep sleep, from which he awoke in the late afternoon to eat a huge meal. He was conscious of having been in some unpleasant psychical

state but the details were fast-fading . . . though not from his wife's memory.

Comment. Because the big majority of patients bothered by threadworms are young children, the possible, perhaps even probable, distressing reaction to promethazine given in a single large dose by mouth, described above, cannot be anything but a serious contra-indication to its use in a family practice where the doctor-patient friendship might be somewhat strained.

SUMMARY

A method of treating threadworm infestation by a single dose of promethazine hydrochloride is described and discussed. A cautionary tale is told to warn against a serious contra-indication.

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IN MEMORIAM

Professor F. O. Fehrsen

Dr. T. Shadick Higgins of Cape Town, writes: The death took place on 24 June 1958 at the Rondebosch and Mowbray Cottage Hospital, Rosebank, Cape, after a short illness, of Dr. Frederick Oloff Fehrsen, who was Medical Officer of Health of the City of Cape Town from 1944 to 1952 after having served as Assistant and Deputy Medical Officer of Health from 1931. For the 8 years during which he was M.O.H. Dr. Fehrsen held the position of part-time Professor of Public Health in the University of Cape Town, and after his retirement in 1952 he was appointed as Emeritus Professor. While District Surgeon of Cape Town he held the position of Lecturer in Medical Jurisprudence at the University for 3 years.

Professor F. O. Fehrsen

The Fehrsen family has been resident in South Africa for over 150 years. Dr. Fehrsen's father, grandfather and great-grandfather were all medical practitioners and he had a number of other relations in the medical profession. His grandfather, Dr. Oloff Fehrsen, who practised in Cape Town, Graaff-Reinet, Cradock and Somerset East, was one of the earliest of those who proceeded to Britain in the 19th century to qualify in medicine.

Fehrsen was born at Middelburg, Cape, and spent much of his boyhood at Somerset East, where he went to school at Gill College. From there he went to Stellenbosch University for a year, when he lived with his uncle Professor John Marais, father of Dr. D. P. Marais, of Cape Town, and in 1911 he proceeded to London, where he took his medical training at the London Hospital.

His undergraduate course was interrupted in 1914, when he went to France in the British Expeditionary Force in World War I as N.C.O. in the Royal Army Medical Corps. After 2 years he was sent back to the London Hospital, where he qualified M.R.C.S. (Eng.), L.R.C.P. (Lond.) in 1916, and after completing resident appointments there he joined the Royal Navy as surgeon-lieutenant. He was on the South Atlantic Patrol for the remainder of the war and was back in South Africa in 1919.

He was appointed Port Health Officer in Cape Town and shortly afterwards was in general practice at Beaufort West until 1925, when he returned to Cape Town as Port Health Officer. From that time Fehrsen devoted himself exclusively to the public medical service. He obtained the Diploma of Public Health at Cape Town University and held the position of full-time District Surgeon, Cape Town, for 3 years. He was appointed Assistant Health Officer for the Union, holding this position at Pretoria for about a year, after which he resumed the post of District Surgeon, Cape Town.

In 1931 Dr. Fehrsen was appointed Assistant M.O.H. for the City of Cape Town, succeeding as M.O.H. in 1944 and holding that position until he reached the age of retirement in 1952.

Although by the nature of his work much of Fehrsen's time was taken up by administrative measures, clinical medicine always remained his first love, and he was ever an assiduous reader of medical journals, especially the *British Medical Journal*.

I was first brought into close contact with Fehrsen when he took my D.P.H. course at the Cape Town University in 1926, and after his appointment as my colleague in the municipal service in 1931 we worked closely together until my retirement from the position of M.O.H. in 1944. Fred Fehrsen was beloved by a wide circle of friends. He had endless stores of amusing stories and both at work and socially he was a man whose company was a delight. To me he was an able and loyal colleague and a true friend. As M.O.H. he distinguished himself in epidemiological investigation. Two important pieces of work that he brought to a successful conclusion were the introduction into Cape Town of compulsory pasteurization of the public milk supply, and the establishment of the Central Dental Clinic at Hope Street, Cape Town, where under-privileged persons of any race, sex or age can obtain dental services (extractions, fillings, and dentures) free or at charges within their means.

After retiring from the municipal service he worked successfully for a number of years on the medical staff of the Valkenberg Mental Hospital, Cape Town, where, indeed, he was still employed when overtaken by his fatal illness.

Dr. Fehrsen was an active member of the Medical Association of South Africa. For many years he was a member of the Cape Western Branch Council and in 1949 he held the position of Branch President. Until he withdrew before last year's election he was a member of Federal Council.

He was a keen sportsman and was for many years a most popular member of the Mowbray Golf Club. At the London Hospital he played rugby and cricket and distinguished himself in athletics.

He is survived by his widow and 3 children, Mr. Oloff Fehrsen, Mrs. Marie Green and Mrs. Laura Whitaker, all of Cape Town.

The funeral service was conducted by Rev. J. W. Aubrey at St. Saviour's, Claremont, and at the Crematorium, Maitland. The church was filled by a large congregation, comprising the Town Clerk (Mr. F. G. Gale) and Deputy Mayoress (Mrs. Newton Thompson) of Cape Town, and many medical colleagues. The bearers and pall-bearers included Drs. B. Bromilow-Downing, T. E. Cheze Brown, E. C. Crichton, J. A. Currie, J. P. de Villiers, T. Shadick Higgins, A. W. S. Sichel, A. Stewart and A. M. C. Whitaker.

Dr. A. P. Blignault, of Cape Town, writes: The sudden death of Dr. F. O. Fehrsen came as a great shock to all who had known him over a period of years. His passing leaves those of us who had the privilege of working with him, with a sense of irreparable loss. A jovial and genial colleague has passed away.

Abundant warmth, great sincerity and a strong sense of devotion to such public services as he was called upon to render, characterized his personality. In addition to his official duties as M.O.H. for Cape Town, he served the Medical Association faithfully as an enthusiastic member of Federal Council and of the Head Office and Journal Committee.

What one especially admired in him was his capacity for entering into and sharing the feelings of other, less fortunate, people without ever losing the lighter touch. The mischievous twinkle in his eye—his readiness to see the humorous in every situation—was his most endearing quality.

I was one of the many students privileged to have Dr. Fehrsen as a lecturer in public health. He served the medical school of Cape Town in this capacity for several years and was greatly loved by many generations of students for his ready wit, his easy and infectious humour and his broad humanity.

After he retired he joined the staff of Valkenberg Hospital where he was working at the time of his death. He soon became so keenly interested in the 'cause' and practice of psychiatry that the administration of some of the most difficult modern methods of treatment could be entrusted to him. Valkenberg Hospital can ill afford to lose him and this country can ill afford to lose citizens of the professional, moral and human stature of Dr. Fehrsen.

We can assure his wife and family that their great sorrow is shared by many others.

DEGREES CONFERRED AT THE UNIVERSITY OF CAPE TOWN

The following degrees in the Faculty of Medicine were conferred at a Congregation of the University of Cape Town on 27 June 1958:

Doctor of Medicine

Hymie Gordon, B.Sc., M.B., Ch.B. (Subject of Thesis: 'Studies on the regulation of the serum-cholesterol level in man, with particular reference to dietary factors').

Barry Lewis, B.Sc., M.B., Ch.B., Ph.D. (Subject of Thesis: 'Studies in Cholesterol metabolism').

Master of Medicine (*Anaesthetics*)

Leonard Rogers Bingham, M.B., Ch.B. (Pret.).
Petro Henriette Malherbe, M.B., Ch.B.

Master of Medicine (*Obstetrics and Gynaecology*)

Harold Freiha Mukheibir, M.B., Ch.B.

Master of Medicine (*Ortorhinolaryngology*)

Peter Packer, M.B., Ch.B.

Master of Medicine (*Surgery*)

John Ronald Clacey, M.B., Ch.B.

Bachelor of Medicine and Bachelor of Surgery

Kemal Eshaam Abdurahman.
Samuel Morris Basker.
Michael Bleiman.
Ebenezer Reginald Botha.
Ernst Philippus Bouwer.
Fred Danziger.
Roy Gordon.
Ronald William Joshua.
Christian Landman.
Abdullah Eshaak Mohamed.
Ivan James Nurick.
Arthur Brian Rosenberg, B.Sc. (Stell.).
Robert Charles Irvin Sandell, BSc.
Oscar Michael Segal.
Louis Wilhelm Stassen.
*Marthinus Louis Steyn.

UNIVERSITY OF THE WITWATERSRAND : SIXTH PROFESSIONAL EXAMINATION FOR THE DEGREE OF M.B., B.Ch.

The following candidates have completed all the requirements of the Sixth Professional Examination for the degree of M.B., B.Ch.:

Bwanausi, H. W.
Dendar, M.
Falcke, H. S. M.
Grisdale, H. S.
Jajbhay, M.
Mpamba, Y. M.
Nombe, W. W. W.
Opperman, A. F. C. L.
Rabie, S. P. A.
Rubin, A.
Sherman, Y.
Silver, J.
Voges, D. P.

PASSING EVENTS : IN DIE VERBYGAAN

Mr. Wilfred Kark, F.R.C.S. has changed his consulting rooms from 33 Jenner Chambers to 46 Lister Buildings, Jeppe Street, Johannesburg. The telephone numbers remain unchanged, viz. rooms 23-9560, residence 41-1605.

* * *

Dr. Lewis S. Robertson was unanimously re-elected Chairman of the Johannesburg Hospital Board on 27 June 1958.

Dr. Lewis S. Robertson is op 27 Junie 1958 eenparig herkies tot Voorsitter van die Johannesburgse Hospitaalraad.

* * *

Dr. Lionel Stein has returned from a 3 month visit to England and the Continent, and has resumed practice as a Specialist Physician at 308 Medical Centre, Cape Town.

Dr. Lionel Stein, is terug van 'n besoek aan Engeland en die Vasteland wat 3 maande geduur het; hy sit weer sy praktyk as Spesialis-Internis voort te Mediese Sentrum 308, Kaapstad.

* * *

Dr. B. A. Bradlow, who has spent 3 months visiting clinics and hospitals in Britain and on the Continent, returned to Johannesburg on 4 July 1958.

Dr. B. A. Bradlow, wat 3 maande lank klinieke en hospitale in Brittanje en op die Vasteland besoek het, het na Johannesburg teruggekeer op 4 Julie 1958.

* * *

Dr. I. Henkel, M.B., Ch.B., M.Med.(Chir.) (Pret.), M.D. (Bonn), het begin praktiseer as 'n Ortopediese Chirurg te Mediese Sentrum 414, Pretoriusstraat, Pretoria op 1 Julie 1958. (Telefoon 3-6938).

Mr. I. Henkel, M.B., Ch.B., M.Med.(Chir.)(Pret.), M.D. (Bonn), commenced practice as an Orthopaedic Surgeon at 414 Medical Centre, Pretorius Street, Pretoria on 1 July 1958. (Telephone 3-6938.)

* * *

Drs. Samuel, Komins, Denny, de Villiers and Berezowski (radiologists), wish to inform their colleagues that they have opened X-ray consulting rooms for out-patients on the third floor, Clarendon Centre, 4 Park Lane, Johannesburg.

Drs. Samuel, Komins, Denny, de Villiers en Berezowski (radioloë) wens hulle kollegas in kennis te stel dat hulle spreekkamers vir X-straal-ondersoek van buitepasiënte, op die derde verdieping te ,Clarendon Centre', Parklaan 4, Johannesburg, geopen het.

* * *

Mr. A. Singer returned to Cape Town on 30 June 1958 having been overseas for the past 2 months. He attended the orthopaedic conference in Washington and after this visited Great Britain and the Continent.

Dr. A. Singer het op 30 Junie 1958 in Kaapstad teruggekeer na 'n reis oorsee gedurende die afgelope 2 maande. Hy het die ortopediese konferensie te Washington bygewoon en Groot-Brittanje en die Vasteland daarna besoek.

* * *

Dr. Ben Epstein of Pretoria has been elected a Foreign Corresponding Member of the American Academy for Cerebral Palsy. Dr. Epstein will attend a special study course on Child Neurology which will be held in Oxford at the end of September 1958. The course has been organized by the International Study Group of the National Society for the Welfare of Spastics, who have invited representatives from various countries to attend. Dr. Epstein is Vice-Chairman of the Cerebral Palsy Division of the National Council for the Care of Cripples in South Africa, and Chairman of the Board of Management of the Pretoria School for Cerebral Palsy.

* * *

Transport of Premature Infants in the Cape Peninsula. The Cape Peninsula Ambulance Station is now equipped with special cribs for the transport of premature infants. These cribs are lined, fitted with hot-water bottles and Perspex covers. When telephoning the Ambulance Station, practitioners should state that the patient is a premature infant, and that a crib is required.

Vervoer van Voortydige Kinders in die Kaapse Skiereiland. Die Ambulans-stasie van die Kaapse Skiereiland is nou uitgerus met spesiale kinderbedjies vir die vervoer van voortydige kinders. Hierdie bedjies is uitgevoer en uitgerus met warmwaterbottels

en Perspex-oortreksels. Wanneer praktisyns die Ambulansstasie bel, moet hulle sê dat die pasiënt 'n voortydige kind is en dat 'n bedjie nodig is.

* * *

The Gairdner Charitable Foundation of Toronto, Canada, announces 2 types of international award. The first, an award of merit, is a 4-yearly prize of 25,000 dollars for the individual or group of workers who in the Foundation's view have made the most outstanding contribution in the fields of arthritic, rheumatic and cardio-vascular diseases. The second type of award consists of a series of prizes of 5,000 dollars for up to 5 persons a year for contributions in the same field.

Awards will be made solely in the discretion of the Foundation. Further details may be obtained from the general secretary, Gairdner Charitable Foundation, 320 Bay Street, Toronto, Canada.

* * *

Medical Directory—Knox Printing Company. At the recent meeting of the Federal Council the question was raised whether it would be ethical for a medical practitioner to supply details requested for inclusion in a medical directory to be published by the Knox Printing Company, of Durban. Apparently this matter had been placed before the S.A. Medical and Dental Council for an opinion, and the Council had agreed that there was no reason why the particulars should not be furnished, 'provided that the material was not presented in such a manner as to cause the individual to contravene the Council's rules and more especially those rules relating to advertising'. The Federal Council agreed with this opinion and further agreed 'that a notice be published in the *Journal*, pointing out that it would not be unethical to supply the necessary details for publication in a medical directory'.

* * *

Die Jaarlikse Karl Bremer-hospitaalstafdag vind vanjaar op 5 September 1958 in die Burgersentrum te Bellville plaas. Referate en uitstallings i.v.m. navorsingswerk sal gelewer word deur die geneeskundige personeel van die Karl Bremer-hospitaal en dosente van die Fakulteit van Geneeskunde van die Universiteit van Stellenbosch. Alle geneeshere en belangstellendes is welkom om die verrigtinge van die dag by te woon. Verversings word aangebied. Daar sal ook uitstallings deur Farmaseutiese Maatskappye gereël word. 'n Volledige program sal later gepubliseer word.

The Annual Karl Bremer Hospital Staff Day will take place this year on 5 September 1958 at the Civic Centre, Bellville. Lectures and exhibits in connection with research work will be delivered by the medical personnel of the Karl Bremer Hospital and the lecturers from the Faculty of Medicine of the University of Stellenbosch. All doctors and people interested are welcome to attend the proceedings of the day. Refreshments are offered. Exhibits by Pharmaceutical Companies will also be arranged. A full programme will be published at a later date.

* * *

Unie van Suid-Afrika. Departement van Gesondheid. Aangifte van gedugte epidemiese siektes en poliomiëlitis in die Unie gedurende die tydperk 20 tot 26 Junie 1958.

Pes, Pokkies, Tifuskoors. Geen.

Poliomiëlitis

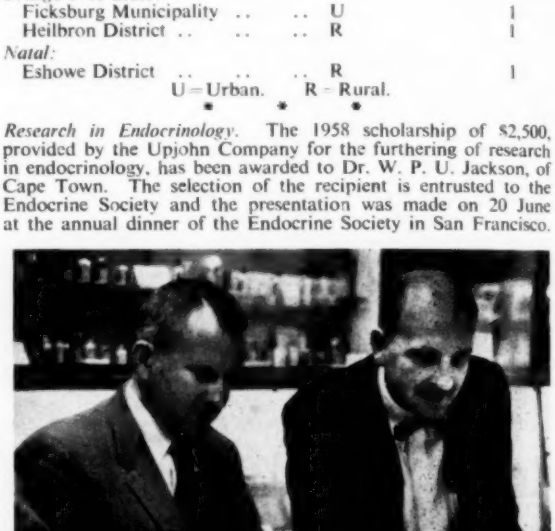
	Bl.	*Nat.*	*Kl.*	*As.*	*Totaal*
Transvaal	3	–	–	–	3
Kaapprovinsie ..	2	5	2	–	9
Oranje-Vrystaat ..	–	2	–	–	2
Natal	–	1	–	–	1
Totaal ..	5	8	2	–	15

Local Authorities		*Eur.*	*Non-Eur.*
Transvaal:			
Johannesburg Municipality ..	U	3	
Cape Province:			
Cape Divisional Council	U	1	
Despatch Municipality	U		1
Paarl Municipality	U		1
Port Elizabeth Divisional Council	U	1	
Port Elizabeth Municipality ..	U		1
Steytlerville Divisional Council ..	R		1
Uitenhage Municipality	U		2
Willowmore Divisional Council ..	R		1
Orange Free State:			
Ficksburg Municipality	U		1
Heilbron District	R		1
Natal:			
Eshowe District	R		1

U = Urban. R = Rural.

* * *

Research in Endocrinology. The 1958 scholarship of $2,500, provided by the Upjohn Company for the furthering of research in endocrinology, has been awarded to Dr. W. P. U. Jackson, of Cape Town. The selection of the recipient is entrusted to the Endocrine Society and the presentation was made on 20 June at the annual dinner of the Endocrine Society in San Francisco.



Dr. W. P. U. Jackson (right of picture) with Dr. Fenimore T. Johnson, Medical Director of Upjohn International Operations, Inc.

Dr. Jackson is a full-time physician in the Department of Medicine, Cape Town University. His work in the field of prediabetes, particularly the detection of individuals who are prone to eventually develop diabetes, has attracted world-wide recognition. Former recipients of the Endocrine Society's Upjohn award have included Dr. Fuller Albright of Harvard University and Dr. Rachmiel Levine of the University of Chicago.

NEW PREPARATIONS AND APPLIANCES : NUWE PREPARATE EN TOESTELLE

STERASYL KIESELGUHR FILTERS

British Berkefeld Filters Ltd. are introducing the Sterasyl Kieselguhr Filters and submit the following information:

Kieselguhr has for many years been employed as a filtering medium for domestic and industrial filters. This silicious earth owing to its porous nature forms a highly efficient filter. It is used in Berkefeld filters in the form of hollow candles which allow the water to pass through from outside to the inside leaving all impurities on the outer surface and giving a high degree of bacteriological purification. To maintain this condition, however,

the candles must be removed from the filter periodically and sterilized by boiling; otherwise bacteria would tend to develop in the sediment collected on their exterior.

To overcome this disadvantage research was carried out some years ago with soluble disinfectants incorporated in the candles with a view to providing these with a sterilizing action which would endure throughout their entire life. The irregular rates of filtration, however, and consequent variation in the amount of sterilant absorbed by the water made this method impracticable.

Experiments recently carried out with finely divided silver showed that if this could be effectively introduced, the bactericidal properties of the silver ions would produce a more lasting sterilizing action. Silver is one of the least poisonous of metals and the amount which water can absorb is very small.

An efficient process was finally devised to ensure thorough and uniform penetration of the silver into the kieselguhr candles and subsequent tests lasting for 2 years showed that water which was artificially contaminated to a degree such as would never be encountered in any supply provided for domestic purposes was made safe for drinking by a single passage through the candle. Furthermore, the water so treated could be stored for considerable periods without bacteriological deterioration.

Since the development of this type of candle (to which the name 'Sterasyl' was given) every test made has shown complete absence of *Bacillus coli* in the filtered water and the life of the candles has been recorded as being upwards of 2 years. Spore bacilli and algal growth, which are resistant to normal sterilizing agents, are also destroyed by the Sterasyl process.

Official tests subsequently carried out by public health authorities with Sterasyl candle filters in various parts of the world under the most arduous conditions and with a large variety of bacteriological organisms have confirmed in every case their complete bactericidal action.

The only maintenance required is occasional cleaning with a soft brush in clean water when the rate of filtration shows signs of slowing down. No soap or other detergent is necessary. Filters incorporating these candles have been proved to be equally efficient in tropical climates.

Further details may be obtained from the manufacturers, British Berkefeld Filters Ltd., Sardinia House, Kingsway, London, England.

CHANGE OF DISTAQUAINE V 120 MG. AND 240 MG. TABLET STRENGTHS

British Drug Houses (S.A.) (Pty.) Ltd. supply the following information:

Phenoxymethylpenicillin (Distaquaine V, penicillin V) has become an official product of the British Pharmacopoeia 1958. The monograph states a dose range of 125 mg. to 250 mg. and for this reason British Drug Houses announce that Distaquaine V 120 mg. and 240 mg. tablets will in future be available to conform with B.P. requirements as 125 mg. and 250 mg. strengths. The 60 mg. tablets and the two Distaquaine V Elixirs will remain unchanged. The D.Q.V. range will therefore consist of the following preparations: Distaquaine V 60 mg. Tablets, Distaquaine V 125 mg. Tablets, Distaquaine V 250 mg. Tablets, Distaquaine V Sulpha Tablets, Distaquaine V Elixir, Distaquaine V Elixir Forte.

REVIEWS OF BOOKS : BOEKRESENSIES

BRITISH PHARMACOPOEIA 1958

British Pharmacopoeia 1958. Published under the direction of the General Medical Council. Pp. xxvi + 1012. 63s. net. London: The Pharmaceutical Press. 1958.

(This new edition will be published on March 3 and become official on September 1, 1958. It will supersede the B.P. 1953 as amended by the Addendum 1955.)

It is accepted by all that there has been remarkably rapid progress in pharmacological and pharmaceutical knowledge in recent years. As a result the interval between publications of the British Pharmacopoeia has been reduced to a period of 5 years, and within these periods an addendum is published. The authorities responsible for this official book, the contents of which have legal sanction, and are of course most important for the medical profession, have had great difficulty in selecting drugs for inclusion in this volume. There are many new synthetic and biological substances that have been introduced into medicine; many are of complex composition for which precise and elaborate analytical procedures have to be provided in framing the standards.

In this edition much effort has been made by numerous workers to provide carefully prepared monographs and the book is a model of accuracy and presentation. Among the principal changes that have been made only brief hints can be given. There is avoidance of long titles for preparations e.g. Neostigmine Injection for Injection of Neostigmine Methylsulphate; Opium Tincture for Tincture of Opium. There is a long list of additions to the pharmacopoeia, covering a wide range of synthetic drugs, antibiotics, hormones, and biological materials, and preparations such as injections and tablets. An interesting list is that of the deletions indicating the exclusion of some 136 preparations, such as amyl-nitrite, butacaine sulphate, calcium phosphate, chenopodium oil, cinchophen, diphenan, hexobarbitone, lamellae, ointment of boric acid, ointment of penicillin, pamaquin, phenadoxone, phenylbutazone, sulphathiazole, suppositories, tincture of digitalis, and a number of injections and tablets. In some cases titles have been changed e.g. chlortetracycline is the approved name for aureomycin, diphtheria vaccine for diphtheria prophylactic, tetanus vaccine for tetanus toxoid, and there are also certain alterations in composition and strength in certain instances. Details are given for the manufacture of injections, tablets, capsules, and for serological and immunological products. Assays for chemical substances include the most advanced analytical techniques. There are monographs on certain radioactive preparations.

This guide for manufacturing chemists and those who prescribe approved drugs will be studied in detail especially in the pharmaceutical industry and by teachers in medical schools, but interested physicians will also find much of interest and importance in perusing its pages.

N.S.

RADIOLOGICAL PHYSICS

Radiological Physics. By M. E. J. Young, M.Sc. Pp. x + 365. 184 Illustrations. £2 2s. net. London: H. K. Lewis & Co. Ltd. 1957.

Contents: I. Introduction: Fundamental Concepts. II. Thermionic Emission and Electronic Valves. III. The Production of X-rays up to about 400 keV. in Energy. IV. The Production of High Energy X-rays. V. Naturally-occurring Radioactive Substances and their use as Sources of Ionising Radiation. VI. The Interaction of X- and γ-Radiation with Matter. VII. The Measurement of Ionising Radiations. VIII. The Measurement of Ionising Radiations (continued). IX. Physical Principles of Diagnostic Radiography. X. Some Chemical and Biological Effects of Ionising Radiations. XI. The Therapeutic Use of X- and γ-Radiation. XII. The Therapeutic Use of X- and γ-Radiation (continued). XIII. Nuclear Structure and the Production and Medical Use of Artificial Radioactive Isotopes. XIV. Health Hazards and Radiological Protection. Useful data. Index.

This book adequately fulfils the author's aim. He has set out to cater for the requirements of the examinations for the Society of Radiographers of Great Britain and for the Diplomas in Radiology, both in diagnosis and therapy.

The elementary classical physics, usually encountered in textbooks of this nature, has been omitted. A sound balance has been maintained in the presentation of a simple but adequate theoretical background and its practical clinical applications.

Modern equipment and techniques are lucidly described and this book is abreast of present day trends in all aspects of radiological physics. The arrangement is logical and the clarity with which this book is written explains, clearly, certain concepts which are by no means easy to understand for radiographers and medical post-graduates by whom much of physics learnt earlier has been forgotten. The 14 chapters adequately cover the various aspects of X-ray and gamma-ray absorption, measurement of ionising radiations, the various types of ray counters, megavoltage units, isotope teletherapy units and diagnostic radiography.

Other useful and interesting chapters include radiological protection, the chemical and biological effects of radiation and detailed accounts of the application of radio-active isotopes in diagnosis and therapy.

Good cross references are a feature of the book.

Of considerable value to the student are questions extracted from the M.S.R., F.S.R. and D.M.R. examinations at the end of each

chapter. This book is highly recommended to those sitting for the above examinations as well as to physicists who are preparing for posts in hospital physics departments.

N.J.

TEXTBOOK OF MEDICAL TREATMENT

Textbook of Medical Treatment. 7th Edition. Edited by D. M. Dunlop, B.A. (Oxon.), M.D., F.R.C.P. Ed., F.R.C.P. Lond., Sir Stanley Davidson, B.A. (Camb.), M.D., F.R.C.P. Ed., F.R.C.P. Lond., M.D. (Oslo) and S. Alstead, M.D., F.R.C.P. Ed., F.R.C.P. Lond., P.R.F.P.S. Pp. xix + 924. IV Plates. 27 Figures. 55s. net + 3s. Postage Abroad. Edinburgh and London: E. & S. Livingstone Ltd. 1958.

Contents: Infectious Diseases. Chemotherapy. Corticotrophin and Cortisone. Anticoagulant Therapy. Dehydration and Electrolyte Deficiencies. Tuberculosis. Common Diseases of the Skin. Venereal Diseases. Common Tropical Diseases and Helminthic Infections. Some Common Disorders in Infancy and Early Childhood. The Care of Old People. Industrial Diseases. Diseases of the Ductless Glands. Disorders of the Blood. Chemotherapy in Malignant and Allied Diseases. Diseases of the Alimentary System. Diseases of the Heart and Circulation. Diseases of the Blood Vessels of the Limbs and the Effects of Cold. Diseases of the Nose, Throat and Ear. Diseases of the Respiratory System. Renal Diseases. Chronic Rheumatic Diseases and Diseases of Bone. Psychotherapy in General Practice. Diseases of the Nervous System. The Welfare of the Disabled. Treatment of Poisoning. Technical Procedures. Principles of Prescribing.

The appearance of the seventh edition of this trusty manual on medical treatment is both a testimony to the rapid progress in therapeutics over the last twenty years and to the place that this textbook has come to occupy in the affections of the medical public.

In the latest edition, which has been extensively revised, three new chapters have been added. These include a section on Corticotrophin and Cortisone, one on the principles of prescribing and an excellent chapter summing up the present status of anticoagulant therapy. For the rest, the book continues to reflect the conservative approach of the Scottish school of Medicine. It is, for instance, somewhat surprising to find that judgement is still suspended on the relative merits of intramuscular and intravenous iron for parenteral therapy. In addition, no mention is made of the possible place of cobalt in the treatment of certain anaemias in spite of a large body of literature on both topics. Although most subjects are covered in some detail more attention might well have been given to the management of barbiturate poisoning and to the so-called 'Tranquillizers' while a section on the approach to intractable pain would be helpful.

In a book by many authors it is inevitable that there should be some degree of overlap between chapters. Thus the therapy of lymphomas is discussed in two separate sections. On the whole, however, editing has been good and there is a useful cross-index system. It is always tempting to gild the lily but one wonders whether the addition of a selected bibliography would not enhance the value of future editions.

A recommendation of this book is very much like preaching to the converted. The consistently high standard of the present edition should ensure that it continues to find a place on the bookshelves of most senior students and practising doctors.

T.H.B.

ANIMAL DISEASES IN SOUTH AFRICA

Animal Diseases in South Africa. Third Edition (Completely Revised). By Michiel W. Henning, M.R.C.V.S., D.Sc. Pp. xv +1,239. 152 Illustrations. £5 10s. 0d. Johannesburg: Central News Agency Ltd. 1956.

Contents: Foreword to Second Edition. Preface to Second Edition. Preface to Third Edition. *Section I. Bacterial Diseases.* A. *Diseases Caused by Aerobic Bacteria.* 1. Anthrax, Miltsiekte. 2. Brucellosis, Contagious Abortion, Brucella Abortion. 3. Tuberculosis (Consumption, Phthisis, Tering). 4. Johne's Disease. 5. Strangles, Nuwesiekte. 6. Glanders, Farcy, Droes, Malleus. 7. Meliodosis. 8. Actinomycosis, Actinobacillosis and Dermatomycosis or Lumpy-wool (either an aerobic or an aerobic bacteria). 9. Cryptococcus Infection. 10. Pleuro-pneumonia Contagiosa Bovium, Lung-sickness of Cattle, Longsiekte. 11. Mastitis. 12. Diseases of Newborn Animals. 13. Vibrio Foetus Infection. 14. Spirochaetosis of Pigs. 15. Leptospirosis. 16 Swine Erysipelas. 17. Atrophic Rhinitis. B. *Diseases Caused by Anaerobic Bacteria.* 1. Blackquarter, Blackleg, Quarter-evil, Sponsiekte. 2. Clostridium Septicum Infections. 3. Clostridium Oedematiens Infections. 4. Clostridium Welchii Infections. 5. Botulism, Lamsiekte. 6. Tetanus, Lockjaw, Klemkaak. *Section II. Protozoal Diseases.* 1. Redwater, Texas Fever, Rooiwater. 2. Gallsickness, Galsiekte (Anaplasmosis). 3. Eperythrozoonosis. 4. The Theilerioses including East Coast Fever, Tzaneen Disease and Corridor Disease. 5. Biliary Fever or Malignant Jaundice in Dogs. 6. Biliary Fever in Horses (Equine Piroplasmosis). 7. Porcine Babesiosis. 8. Coccidiosis (Bloody Diarrhoea) of Calves. 9. Globidiosis (Olifantvel). 10. Trichomoniasis, Trichomonas Disease of Cattle. 11. Trypanosomiasis. *Section III.* Diseases caused by Viruses and Rickettsias. 1. African Horsesickness, Perdesiekte, Pestis Equorum. 2. Blue-tongue. 3. Rinderpest, Cattle Plague, Runderpes. 4. Swine Fever, Hog Cholera, Varkpes. 5. Foot-and-Mouth Disease, Mond-en-Klouseer. 6. Canine Distemper, Hondesiekte and Infectious Canine Hepatitis or Rubarth's Disease. 7. Rabies, Hydrophobia, Hondsdolheid. 8. Knopvelsiekte, Lumpy-skin Disease. 9. Snotsiekte (Malignant Catarrh) in Cattle. 10. Ephemeral Fever. Three-day-sickness, Drie-Daesiekte. 11. Equine Epizootic or Infectious Abortion. 12. Equine Influenza or Pink Eye. 13. Infectious Virus Pneumonia of Pigs and Swine Influenza. 14. Sweating Sickness, Sweetsiekte. 15. Blouwildebeesoog, Uitpeuloog. 16. Rift Valley Fever. 17. Nairobi Sheep Disease. 18. Infectious Bovine Infertility (IBI), Besmetlike Onvrugbaarheid van Beeste (BOB). 19. Infectious Equine Anaemia. 20. Heartwater, Hartwater. 21. Rikettsiosis of Dogs. 22. Specific or Infectious Ophthalmia. 23. Q Fever. 24. Infectious Abortion of Ewes.

The third edition of this extremely valuable book will be greatly welcomed in both veterinary and medical spheres. Probably one of the best works on veterinary diseases the book is a pleasure to read.

The book is divided into 3 large sections: 1. Bacterial Diseases. 2. Protozoal Diseases. 3. Virus and Rickettsial Diseases.

Each chapter gives a historical background of the disease; the etiology is fully discussed, old and modern concepts being reviewed. The causal organism and its cultural characteristics are described, and methods of investigation indicated. The morbid anatomy, pathogenesis of the disease, symptoms and treatment, both preventitive and curative are so fully dealt with that further reading is hardly necessary. When the disease occurs in man the symptoms are described or attention is drawn to reported cases in Man in Africa, e.g. Leptospirosis.

A number of diseases not discussed in the previous editions are now included. Of particular interest to medical men will be the chapters on Rift Valley Fever, Q-Fever and Leptospirosis. Other new chapters include Nairobi Sheep Disease, Porcine Babesiosis, Eperythrozoonosis, Corridor Disease, Ovine Abortion, Virus Pneumonia of Pigs and Seine Influenza. Full references at the end of each chapter add to the value of the book.

Details sufficient to satisfy the most exacting reader are included in the nearly 1,200 pages of this book. Professor Henning is to be thanked and congratulated on a finepiece of work well written and well illustrated.

G.S.

CORTISONE THERAPY

Cortisone Therapy. Mainly Applied to the Rheumatic Diseases. By J. H. Glyn, M.A. (Cantab.), M.D., M.R.C.P., D.Phys.Med. Pp. x+162. 4 Figures. 21s. net. London: William Heinemann —Medical Books—Ltd. 1957.

Contents: Foreword. Acknowledgements. Introduction. 1. Historical Review. 2. The Nature of Cortisone and other Steroid Drugs. 3. Pharmacological Properties and Side Effects. 4. The Practical Problems of Cortisone Therapy. 5. Intra-articular Injections of Cortisone and Hydrocortisone. 6. The Use of Cortisone in Diseases other than Rheumatoid Arthritis. 7. General Discussion. *Appendices.* I. The Anatomy and Technique of Intra-articular and Soft Tissue Injections. II. Assessment of Clinical Progress. III. Further Reading. Index.

This little book contains a fund of useful information on many aspects of cortisone therapy including the important and controversial subject of side effects and complications.

It is pleasing to see that Dr. Glyn is not one of those who consider a history of peptic ulceration an absolute contra-indication to the use of adrenal steroids. Nor does he regard fluid retention, glycosuria and other minor complications as good reason for discontinuing an otherwise effective therapeutic agent.

A little more space could perhaps have been devoted to the phenomenon of 'hypercortisonism' and its treatment, since this complication is not yet sufficiently well recognized and is still being confused with the underlying rheumatoid process. On the other hand, the question of adrenal atrophy resulting from steroid administration is put into correct perspective as a distinctly unusual though highly disturbing complication. One cannot but agree that the use of corticotrophin to stimulate the atrophied adrenal is of questionable value and is not in keeping with what is known of endocrine 'servo' mechanisms.

Much of what Dr. Glyn says is based on personal experience and there are doubtless many who will disagree with some of the views stated. Nevertheless, the book is worth while from many aspects and is highly recommended. It is a pity that a fuller bibliography has not been included.

S.J.F.

HYPERTENSION

High Arterial Pressure. By F. H. Smirk, M.D., F.R.C.P., F.R.A.C.P. Pp. xxxvi+764. Illustrated by figures and plates. 75s. Oxford: Blackwell Scientific Publications. 1957.

Contents. Preface. 1. Introduction. 2. Casual, Basal and Supplemental Blood Pressures. 3. Natural History and Ecology of High and Low Blood Pressure. 4. Influence of Changes in Living Conditions on the Blood Pressure Level. 5. The Clinical Manifestations of Hypertension. 6. Aetiology. 7. Psychosomatic Aspects of High Blood Pressure. 8. The Physiology of Blood Pressure Regulation.

9. Experimental Hypertension. 10. The Relationship between Arteriosclerosis and Hypertension. 11. Pathogenesis of Essential Hypertension. 12. Prognosis of Hypertension. 13. Some Fundamental Principles concerning the Treatment of Hypertension by Blood Pressure Reduction. 14. Surgical Treatment of High Blood Pressure. 15. Severe Salt Restriction. 16. Hypotensive Drugs, mostly of Academic Interest. 17. The Rauwolfia Alkaloids. 18. Pharmacology of Ganglion Blocking Drugs. 19. Treatment of Patients by Ganglion Blocking Agents. 20. Combined Therapy. 21. Results of Treatment. Appendices. Index.

This book is a welcome addition to the literature on hypertension, a disease so common in modern civilisation and yet so baffiing in origin. Despite its size, the facts are so well marshalled and the chapters so arranged that the book reads easily and logically. The author has long been interested in this field and naturally stresses his own views, particularly the importance of basal and supplemental pressures in assessing the severity of hypertension, the prognosis and treatment.

A feature is the extensive bibliography and the clear summaries of our present-day knowledge, regrettably inadequate; but this is no fault of the author. The physiology of blood pressure regulation and the pathological sequelae of a prolonged rise of arterial pressure are fully discussed and, of particular importance, are the chapters on pharmacology of hypertensive drugs and their use in clinical therapeutic regimes.

Not everybody would agree with the treatment of hypertensive cardiac failure by hypotensive drugs alone, nor are the average results in other hands with these drugs as good as those of the author. It is a pity, too, that the renal contraindications to therapy are not adequately discussed. The book can, however, be recommended for its easy style, its fund of references and wealth of material. S.S.

STUDIES ON THE MALARIAL PARASITES

Studies on the Exo-Erythrocytic Cycle in the Genus Plasmodium. London School of Hygiene and Tropical Medicine. Memoir No. 12. By R. S. Bray, B.Sc., Ph.D. Pp. viii + 292. 24 Illustrations. 22s. net. London: H. K. Lewis & Co. Ltd. 1957.

Contents: Preface. List of Figures. 1. Definitions, General Classification. Terminology. 2. Introduction. 3. Historical. 4. The Present State of the Knowledge of the Exo-Erythrocytic Cycle of the Avian and Saurian Plasmodia. 5. The Present State of the Knowledge of the Exo-Erythrocytic Cycle of the Mammalian Plasmodia. 6. Taxonomy and Specific Classification. Bibliography.

Dr. Bray completed this Memoir in 1953, and although there was a delay of almost 4 years before publication in 1957 it remains an accurate and adequate account of our present-day knowledge of this intriguing aspect of the life cycle of the malaria parasite. The past 4 years have seen much additional work in this field, most of it, however, consolidatory in nature and none of it significantly altering the value of Dr. Bray's monograph as an up-to-date account of the subject. A brief set of definitions of terms employed in the description of the third and non-erythrocytic cycle of the malaria parasite is followed by a historical review. This makes fascinating reading and is conveniently divided into three sections covering the gradual realization that a non-erythrocytic cycle probably existed, it's discovery in avian malaria, and culminating in the demonstration of a tissue phase of the parasite in mammalian malaria.

The historical review is followed by descriptions of the morphology of the pre-erythrocytic and exo-erythrocytic cycles of the parasite in firstly avian and secondly mammalian malaria. In describing the latter Dr. Bray gives prominence to the development of the pre-e and e-e cycles in *Plasmodium cynomolgi* infections; the detailed morphological descriptions are accompanied by excellent camera lucida illustrations. Comments on other species, including *P. vivax*, *P. falciparum* and *P. ovale*, are made in relation to *P. cynomolgi*. The descriptions are enhanced by numerous personal observations and here, as elsewhere in the book one repeatedly realises how refreshing it is to be reading the work of an author well qualified, by virtue of his personal experience, to be writing about his subject.

After a description of the biochemistry of the non-erythrocytic parasites, reference to the chemotherapy, and the relationship of pre-e and e-e cycles to relapses and immunity, the author draws attention to the many lacunae in the general knowledge of the mammalian e-e cycles and indicates the nature of the problems which future research will attempt to solve. The reviewer notes with interest that Dr. Bray himself has recently filled one of these gaps with his demonstration of the one-day-old pre-erythrocytic stage of *P. cynomolgi*.

This excellent monograph covers a fascinating and intriguing development in the field of parasitology, and will be of value to both clinician and laboratory worker in this field. The book is well-bound, the print and type-setting make for easy reading, and the paper is of good quality. These features together with the price are to be highly recommended. T.G.S.

A CONGENITAL EYE DISEASE

Heredo-Retinopathia Congenitalis, Monohybrida Recessiva Autosomalis. A Genetical-Statistical Study. By Carl Henry Alström in Clinical Collaboration with Olof Olson. Pp. 178. 9 Figures. Lund: Lund University. 1957.

Contents: Preface. Introduction. I. Material. II. Ophthalmologic Investigation. III. Genetic-Statistical Analysis. General Summary. Conclusions. Appendix 1-5. Appendix 6. Case Records. List of Tables and Appendices. List of Figures. Bibliography. Pedigree-Charts.

In 1945, the author's attention was drawn by Prof. Torsten Sjogren to the frequency of familial incidence and consanguineous marriages in the parents of inmates of the Tomteboda Institute for the Blind, admitted with the diagnosis of congenital retinochoroiditis. There seemed to be sufficient grounds to believe that there existed a genetically uniform disease group, not previously described. Therefore all patients in this Institution with this diagnosis or diagnosed as amaurosis or amblyopia congenita, of unknown origin, with no visible ophthalmological changes, were investigated; and the records of previous admittances from 1897 were consulted. Many of the amaurosis or amblyopia congenita group when re-examined showed retinochoroidal changes and many appeared as secondary cases in the proband families. Thorough neuro-psychiatric and ophthalmological examinations were undertaken and subsequently field examinations over the whole of Sweden were instituted. Numerous figures and tables demonstrate the thoroughness with which the investigations were carried out. Analysis of this work showed that there was indeed a familial incidence and a high frequency of consanguineous marriage in a disease characterised by probable congenital defect of sight, consisting either of total amaurosis or of greatly impaired sight with loss of central vision, where at an early age scanty or no fundus changes are seen despite the highly defective vision, and with increasing age, 'chorioretinitis' may develop until possible widespread atrophy becomes noticed. There is an absence of neuropsychiatric and endocrinological complications, though cataract and keratoconus present a surprisingly high incidence.

Though this appears at first sight to be a dull subject, the exposition is so clear and precise that reading is simple. There are masses of detail which can be omitted in a cursory examination of the contents. For a statistical study of a genetical entity this book proves an excellent example of thoroughness and preciseness. S.L.

TREATMENT OF ACUTE POISONING

Handbook of Treatment of Acute Poisoning. 2nd Edition. By E. H. Bensley, M.B.E., B.A., M.D., F.A.C.P. and G. E. Joron, B.A., M.D., C.M., F.A.C.P. Pp. xii + 212. 15s. net + 1s. 1d. Postage Abroad. Edinburgh and London: E. & S. Livingstone Ltd. 1958.

Contents: Preface. Acknowledgements. *Section I. Basic Principles, General Plan and Methods of Treatment.* Basic Principles of Treatment: Prevention of further exposure to the poison. Maintenance of a clear airway. Control of respiratory depression. Control of shock. Control of convulsions. Control of infection. Removal and inactivation of the poison General Plan of Treatment: Before arrival of physician. After arrival of physician. Methods of Treatment: Maintenance of a clear airway. Relief of pain. Artificial respiration. Stimulants. Control of convulsions. Oxygen therapy. Gastric lavage. Induction of vomiting. Cathartics. Diuretics. Parenteral fluids. Antibiotics. Chelating agents. Methylene blue. Prevention of oesophagael strictures. *Section II. Important types of Acute Poisoning and Their Treatment.* Acids. Alkalies. Amphetamine and Related Drugs. Aniline and Related Compounds. Anticholinesterases. Antihistaminics. Arsenic. Atropine and Related Alkaloids. Barbiturates. Benzene. Boric Acid and Borates. Botulism. Bromides. Camphor. Cantharidin. Carbon Monoxide. Carbon Tetrachloride and Related Chlorinated Hydrocarbons. Cyanides. DDT and Related Chlorinated Insecticides. Ethyl Alcohol. Ethylene Glycol. Fluorides. Fluoroacetate. Food Poisoning. Gold. Hypnotics. Hypochlorites. Iodine. Iron. Isopropyl Alcohol. Kerosene and Related Petroleum Distillates. Lead. Lung Irritant Gases. Mercury. Methyl Alcohol. Morphine and Related Drugs. Mushrooms. Napthalene. Nicotine. Oxalic Acid and Oxalates. Phenols. Phosphorus. Potassium Permanganate. Salicylates. Strychnine. Turpentine. Warfarin. Xylene. *Appendix.* Emergency Poison Kit. Collection and Preservation of Samples for Chemical Analysis. Bibliography. Index.

All of us, as doctors, may suddenly be called upon to treat a case of acute poisoning whether this be in our practices, in our homes or in the homes of our friends. It is surprising just how many potentially toxic drugs may be encountered during a day. It is a far cry from the days when carbolic acid, arsenic or strychnine were the drugs of choice for suicides (or homicides). Today we are surrounded by the the remains of partly used (and potentially

dangerous) medicines, household solvents, cleaners, and industrial toxins or noxious agents. This little book is designed as a ready reference in cases of acute poisoning and it fulfils this purpose admirably. It has a short general section applicable to most cases of poisoning. (The section on artificial respiration could perhaps include alternative methods of doing this and a few simple diagrams here, as well as when considering stomach lavage, would not come amiss.) Thereafter individual poisons are considered in detail. For each of these there is a short summary of the signs and symptoms, a small section entitled 'Treatment before arrival of physician' (useful for telephoned advice!) followed by a section on 'Treatment after arrival of Physician'. The details are clear and concise. There is a chapter on what one should have available in the 'emergency poison kit'. All in all a book which is well worth while having available. You may not need it for a long time—when you do, you could do with it in a hurry!

C.M.

THE CEREBRAL CORTEX

The Mammalian Cerebral Cortex. By B. Delisle Burns, B.A. (Cantab.), M.R.C.S., L.R.C.P. Monographs of the Physiological Society. Number 5. Editors: H. Barcroft, L. E. Bayliss and A. L. Hodgkin. Pp. vii+119. 25 Figures. 21s. net. London: Edward Arnold (Publishers) Ltd. 1958.

Contents: Preface. I. The general properties of isolated cerebral cortex. II. Afterdischarges. III. The spontaneous activity of central neurones. IV. The transmission of excitation within the cerebral cortex. V. The problem of memory. References. Index.

In this fifth monograph of the Physiological Society the author describes his experiments on the cerebral cortex of the cat. Small portions of cortex were isolated, partially or completely, from the rest of the brain while retaining their blood supply. From the electrical responses of the isolated cortex to local stimulation and to stimulation of the adjacent brain some general conclusions are drawn about spontaneous and induced neuronal activity and about the transmission of nerve impulses in the brain. Theories of facilitation and of learning are explored and an attempt is made to relate the observed activity of the cerebral cortex to its cytoarchitecture.

The experimental work described is ingenious and interesting but admittedly, inconclusive. The monograph relates the author's work to that of other distinguished neurophysiologists and will be read with interest by specialists in this field. The references are well selected and up to date. Unfortunately this highly speculative branch of neurophysiology can offer little guidance as yet to the practising neurologist.

A.W.S.

NEWS LETTER

Newsletter. Edited by E. D. Wittkower, M.D., Section of Transcultural Psychiatric Studies, McGill University, Montreal, Canada. December 1957. No. 3.

For the past three years the Section of Transcultural Psychiatric Studies of the McGill University, Montreal, has been engaged in building up a network of psychiatrists and social scientists interested in establishing information regarding differences in the incidence and nature of mental disorders in relation to socio-cultural background. During this period 3 newsletters have been completed on the basis of the material obtained and have been distributed to psychiatrists and social scientists in many countries.

Some of the major functions of the newsletter are to spread information all over the world; to obtain information which has not yet been published; to acquaint psychiatrists with the nature and range of the problems of other psychiatrists in different countries and 'off-the-beaten-track' places: to establish contact between geographically separated observers; and to stimulate research projects.

In the newsletter under review there are, for instance, notes on the differences in the incidence and nature of mental disorders in Malaya, Thailand, Australia, Arabia, Portugal, Peru, etc.; there are summaries of unpublished material on socio-cultural factors in different countries; information on psychodynamic features related to socio-cultural factors; notes on culture and personality, etc.

This newsletter reflects an interesting awareness of psychiatrists all over the world that the province of psychiatry lies not only in the study of individual patterns of behaviour and of separate disease entities as such, but also in the study of the psychodynamic factors which underlie the thorny problems of human relationships in general.

A fundamental question—with special reference to the great cultural changes and shifts which are taking place all over the world today—as stated by Dr. R. Diaz-Guerrero of Mexico, is 'the question of whether there exist any universal cultural patterns which lead to mental health and others which lead to mental illness, or national cultural patterns that produce such effects'.

The great challenge to psychiatrists today, as well as to all men of good will and common sense is to make as objective a study as possible of human relationships among individuals and groups against the background of divergent personal, social, economic, cultural and political factors.

It is in pursuance of objectives such as these, e.g.: (a) to study ancient patterns of social and cultural life which are deteriorating and disappearing, (b) to enquire into ways of adjustment and integration, (c) to observe the impact of changing conditions on mental health and socio-cultural behaviour, and (d) to note faulty attitudes of the giving and receiving societies—it is with such objectives in view that the Section of Transcultural Psychiatric Studies of the McGill University attempts to enrol the support of as many psychiatrists as possible.

Active support of this newsletter cannot be too strongly recommended. Address all communications to: Section of Transcultural Psychiatric Studies, Department of Psychiatry, McGill University, 1025 Pine Avenue, Montreal, P.Q., Canada.

A.P.B.

AIDS TO MEDICAL DIAGNOSIS

Aids to Medical Diagnosis. 8th Edition. By G. E. Frederick Sutton, M.C., M.D. (Lond.), F.R.C.P. Pp. viii+400. 12s. 6d. London: Baillière, Tindall & Cox Ltd. 1958.

Contents: I. Infectious Diseases. II. Disorders of the Abdomen. III. Diseases of the Blood. IV. Diseases of the Heart and Blood Vessels. V. Diseases of the Lungs and Pleurae. VI. Diseases of the Endocrine Organs. VII. Diseases of the Kidney. VIII. Diseases of the Nervous System. IX. Diseases of the Joints. X. The Electro-Encephalogram. Index.

The ingenuity with which authors in the 'Aids' series manage to provide so much information in so small a compass is always amazing. This new edition of 'Aids to Medical Diagnosis' is no exception. The author, with assistance, has introduced the advances of the last five years by extensive revisions of the text and it is now thoroughly up to date. Students, both undergraduate and post-graduate, will find it to be the real 'aid' that one has come to expect of this series.

T.A.

CORRESPONDENCE : BRIEWERUBRIEK

RODENT ULCER

To the Editor: Without wishing to prolong this correspondence in your columns, I must reply to the main points brought out in Mr. Schrire's letter.[1] He states 'The fact that we can record over 1,000 cases with no deaths in a long follow-up is, we submit, a very satisfactory state of affairs and a tribute to the quality of work and persuasive powers of our radiotherapeutic staff'.

This resounding statement rings hollow to my ears for the type of uncomplicated case submitted for radiotherapy (mainly group 2) does not die anyway. The crux of the matter, and a point on which Mr. Schrire does not touch, is how much morbidity, delay in healing and late tissue breakdown is produced.

Incidently, the cases requiring extensive surgery because of, or in spite of, previous X-ray therapy, came from many parts of the Union (including the Cape) and my letter was not intended as an indictment of radiotherapy in any particular institution or area.

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19 June 1958

1. S.A. Med. J. (1958): 32, 625.